CORONARY-ARTERY PATHOLOGY IN SUDDEN DEATH FROM MYOCARDIAL ISCHÆMIA

A Comparison by Age-groups

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MYOCARDIAL ischæmia in its various forms very commonly causes sudden death; and many medicolegal necropsies are carried out all over the world on these cases. But important gaps still remain in our knowledge of the structural pathology of affected coronary arteries. The detailed pathological anatomy of congenital malformations of the heart became more important when cardiac surgeons developed techniques for treating them; similarly, more detailed knowledge of the coronary arteries is needed now that many cardiologists and surgeons are contemplating direct surgical relief of coronary-artery obstruction. For this we must know, for example, where arterial stenosis most frequently occurs, how much of the artery is likely to be affected, how often several arteries are involved, and the distinctive pattern of the disease in different age-groups. Ischæmic heart-disease in younger men (under the age of 40 years) is often said to differ in some essential way from that in the older age-groups (Acheson 1960, Wright 1960), but little supporting evidence has been recorded. The present investigation was designed to clarify these matters. Recent surveys have reviewed epidemiologically a great many cases (Morris and Crawford 1958); by contrast, we have examined relatively few hearts in greater detail. These two forms of study are complementary.

Material and Methods

The hearts studied were obtained at necropsy from 75 men who had died suddenly; they were not receiving medical treatment. These formed a more homogeneous group than cases coming to necropsy after hospital treatment of varied duration and kind. In these hospital cases the essential coronary changes are often obscured by changes due to cardiac failure of variable duration and severity. To facilitate comparisons, 25 hearts were studied in each of the age-groups 20–39, 40–49, and 50–59 years. The youngest group comprised men aged 24, 26, 28, 30, 32, and 33 years; 2 aged 35; 3 aged 37; 3 aged 38; 5 aged 36; and 6 aged 39.

The hearts were removed unopened at necropsy, and were dissected only after radiographic study of the coronary arteries. For this purpose a simplified technique was employed which outlined the vessels at least as satisfactorily as more complex procedures, and had the great advantages of taking only about 15 minutes to complete, and of leaving the arteries and heart undamaged for subsequent dissection. The proximal parts of the main coronary arteries were dissected free on the outside of the root of the aorta, and ligatures were placed lightly around them. A stabilised micro-dispersion of barium sulphate ('Micropaque', Damancy and Co., Ltd.) was injected first into the right artery through an ordinary 10 ml. syringe with a wide-bore needle. The filling was judged complete when the small branches of the artery on the surface of the heart could be seen to fill, or when an increased resistance to the injection was noted. In most instances about 2 to 3 ml. of opaque medium was required to fill an artery. The needle was then removed, the ligature tied to prevent reflux, and an anteroposterior X-ray taken at a distance of 40 in. with 'Ilfex' non-screened film (50 mA, 60 kV, exposure, 0·5 sec.). The procedure was repeated for the left coronary artery, and a further X-ray was taken. When first using this procedure stereoscopic pairs of films may help, but with a little practice the course of the arteries can be followed quite readily without this added expense. The hearts were subsequently dissected, the X-ray films enabling the stenosed segments of artery to be accurately located. The arteries were sectioned transversely at intervals of 0·5 to 1 cm. along their length, and the stenosed segments were further divided after decalcification and were then cut in serial sections, both freezing and paraffin embedding techniques being used. The whole serial ribbon of sections was not always examined, but sections were taken at ten or more levels from blocks approximately 5 mm. thick. The frozen sections were stained by Sudan III and hæmatoxylin, and the paraffin sections were stained alternately by hæmatoxylin and eosin, the picro-Mallory method, and the Weigert elastic/van Gieson technique. Calcification, the degree of stenosis, and the length of artery involved by confluent atherosclerosis were noted at the time of dissection. The degree of stenosis was finally checked by examining the stained sections and was expressed as the fraction of lumen remaining open. Thus, stenosis of one-quarter means that the area of remaining lumen has been assessed at a quarter of the original. These figures are inevitably only approximate.

Results

In all 75 cases the pathological process which had impaired the blood-carrying capacity of the coronary arteries was atherosclerosis, this term being used to describe the widely prevalent arterial lesion characterised by patchy thickening of the intima, this thickening consisting of accumulations of fat, and layers of collagen-like fibres in widely varied proportions. In many cases fresh or organising occlusive or mural thrombi were present, but these were always on a basis of advanced atherosclerosis. No other pathological basis for the arterial disease was found in any of these cases. The pathological features are tabulated below by age-groups.

Frequency of Occlusion and Stenosis

For simplicity the arterial supply to the myocardium was regarded as consisting of an anterior descending artery, a circumflex artery, and a right coronary artery. The left coronary artery (seldom over 1 cm. in length and often much shorter) was considered as part of the anterior descending artery.

In table I the frequency of recent occlusion and of severe stenosis of one or more arteries is recorded. An occlusion was regarded as recent when unorganised fibrin or atheromatous debris could be identified occupying the former lumen. Stenosis was assessed at two levels: reduction of the lumen to $^1/_3$ of normal, and reduction to $^1/_4$ of normal. Lesser degrees of stenosis were disregarded.

TABLE I—FREQUENCY OF RECENT OCCLUSION AND STENOSIS IN ONE OR MORE ARTERIES

Age-group (yr.)	No. of cases	Recent occlusions (cases)				Stenosis to $^1/_3$ or less (cases)			Stenosis to $^1/_4$ or less (cases)		
		Nil	1 art.	2 art.	3 art.	1 art.	2 art.	3 art.	1 art.	2 art.	3 art.
Under 40 ..	25	7	15	3	..	4	11	10	9	11	5
40–49	25	10	14	1	..	5	8	12	9	9	7
50–59	25	17	6	1	1	5	9	11	7	11	6
Totals	75	34	35	5	1	14	28	33	25	31	18

TABLE II—FREQUENCY AND SITE OF RECENT OCCLUSIONS AND MURAL THROMBI

Age-group (yr.)	Recent occlusions (arteries)						Recent mural thrombi		
	Total art.	L.A.D.	C.	Rt.	By thrombus	By debris	L.A.D.	C.	Rt.
Under 40 ..	21	13	3	5	18	3	1	..	1
40–49 ..	16	9	1	6	11	5	2	..	1
50–59 ..	11	5	2	4	10	1	6	2	..
Totals ..	48	27	6	15	39	9	9	2	2

L.A.D. = left anterior descending artery; C. = circumflex artery; Rt. = right coronary artery.

In all age-groups taken together, single or multiple recent occlusion was found in 41 of the 75 cases; 18 in the under-40s, 15 in the 40–49 group, and only 8 in the 50–59 group.

The differences between the degree of stenosis and the frequency of multiple arterial involvement in the different age-groups are remarkably small, and definitely not significant. No fewer than 61 cases had multiple arterial stenoses down to $^1/_3$ or lower level, and in 49 cases two arteries or more were reduced to $^1/_4$ normal or less.

Sites and Nature of Occlusive Lesions

The frequency in individual arteries of recent occlusion and of recent mural (non-occlusive) thrombosis is shown in table II. The anterior descending artery was the site of 27 of the 48 recent occlusions, and of 9 of the 13 non-occlusive mural thrombi. Of these 36 recent lesions in the anterior descending artery, 9 were at the origin of the descending vessel from the main left trunk, or in the 1st centimetre of its course, 21 in the succeeding 2 cm. (i.e., 1–3 cm. from the origin), and only 6 more distally, the lowest being 5·5 cm. from the origin.

TABLE III—SEVERITY OF PRE-EXISTING STENOSIS AT SITES OF RECENT OCCLUSION

Age-group (yr.)	Pre-existing stenosis			
	0–1/2	1/3–1/5	1/6–1/10	1/12–1/20
Under 40	..	13	6	2
40–49	..	7	8	1
50–59	..	9	2	..
Totals	..	29	16	3

The figures refer to the number of recently occluded arteries showing the stated degree of pre-existing stenosis.

The circumflex artery was the site of 6 recent occlusive lesions, and of 2 mural thrombi; 3 of these 8 lesions were in the 1st centimetre, and 5 were between 1 and 3 cm. from the origin.

In the right artery there were 15 recent occlusions, and 2 mural thrombi. None of these lesions was in the 1st centimetre, 3 were at 1–3 cm. from the vessel's origin, 5 at 3–5 cm., while 9 of the 17 were between 5 and 8 cm. from the origin, forming a very characteristic lesion in the artery after it has passed round the right border on to the back of the heart. The figures do not differ significantly between the age-groups, but there are slightly more lesions in the right artery in older subjects.

Of 48 recent occlusions studied, 39 were due to plugging of the lumen by thrombus, consisting of fibrin with an admixture of blood-cells. The appearance of all was consistent with thrombus formation in situ, and there was no suggestion that embolism had played any part in the process. In the remaining 9 occluded arteries, the plug consisted of atheromatous debris, either alone (2 cases), or mixed with thrombus. All these obstructions by debris were in severely atheromatous segments of artery, so occlusion had probably developed close to the point at which the fatty debris entered the lumen; but the possibility that debris had entered the lumen proximally, and travelled to the site of obstruction as an embolus cannot be excluded.

Hæmorrhages into the substance of the diseased intima were frequently seen, both in occluded and in patent arterial segments, but no intimal hæmorrhage was large enough to close off the lumen.

In table III the degree of stenosis which preceded the recent occlusions is shown. Occlusion was found only in vessels reduced in calibre to one-third or less of the original, and most occlusions were in vessels with lumina between one-third and one-fifth of normal area.

Sites of past occlusion are less easily recognised than those of recent lesions, for many severe eccentric stenoses may well result from organisation of thrombi which, though initially occlusive, have rapidly retracted to one side of the vessel. In the present study lesions were accepted as old occlusions only if either the lumen was plugged by a mass of fibrous or granulation tissue, or recanalisation had resulted in multiple small channels replacing the original lumen. The numbers of these old occlusions found in the different arteries are shown in table IV, together with the totals for old and recent blocks. The old occlusions are much less frequent in the youngest age-group (8 lesions as against 18 and 19), but when old and recent lesions are added together the differences are insignificant. The distribution of the old lesions within the arteries follows the same pattern as that of recent occlusions.

TABLE IV—FREQUENCY OF OLD OCCLUSIONS AND OF OCCLUSIONS OF ALL AGES

Age-group (yr.)	Old occlusions			Occlusions of all ages			
	L.A.D.	C.	Rt.	L.A.D.	C.	Rt.	Total
Under 40	6	1	1	19	4	6	29
40–49	8	5	5	17	6	11	34
50–59	11	3	5	16	5	9	30
Totals	25	9	11	52	15	26	93

Extent of Atherosclerosis

In all these cases the arteries were affected by atherosclerosis (in addition to the stenotic lesions recorded above), but its extent was extremely variable. It was assessed by measuring the length of any artery affected by confluent disease. In many arteries discrete plaques extended for a few centimetres beyond the area of confluent lesions; but this zone was disregarded. The figures are therefore a rough measure of the extent of artery severely affected by atherosclerosis, but they underestimate the total amount of disease. The mean length involved in each artery is recorded for each age-group in table V. The mean total length (last column in the table) demonstrates the expected upward trend with age, but the differences be-

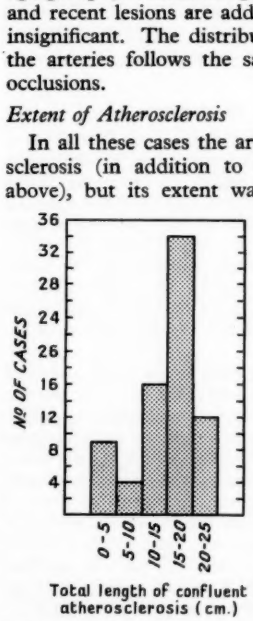

Fig. 1—Frequency distribution of extent of confluent atherosclerosis for each of the 75 cases.

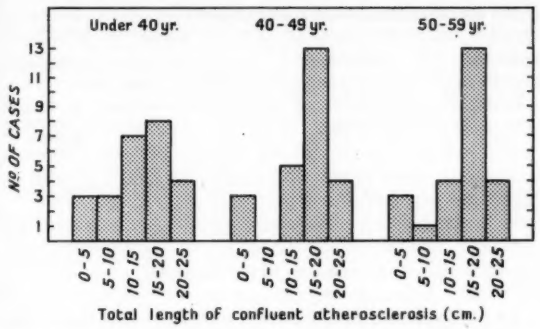

Fig. 2—Frequency distribution of extent of confluent atherosclerosis for each age-group.

tween the means do not quite fulfil the criteria of statistical significance.

The frequency distribution of the different degrees of confluent atherosclerosis is shown in the histograms. In fig. 1 the 75 cases are considered as a single group. 34 of the cases have between 15 and 20 cm. of confluent atherosclerosis, and 62 cases have over 10 cm. involved. From the general shape of this histogram, with a high peak towards the right, few if any cases would be expected in the first block, showing less than 5 cm. of diseased artery. In fact 9 cases come into this category; each age-group includes 3 cases (fig. 2). These 9 cases stand out in the group of deaths from myocardial ischæmia, since atherosclerosis involved such a very short segment of artery. 6 of them had recent thrombi in the short diseased segment of artery, but in 3 the pathological lesion was limited to a short severely stenosed segment. These cases are further discussed below.

TABLE V—EXTENT OF CONFLUENT ATHEROSCLEROSIS

Age-group (yr.)	Mean extent of confluent atherosclerosis (cm.)			
	L.A.D.	C.	Rt.	Total
Under 40	5·1	3·1	5·0	13·2
40–49	5·5	3·2	6·1	14·8
50–59	5·8	3·4	6·1	15·3

Calcification

Only the presence of calcification in an artery was recorded, with no attempt at quantitative measurement. These gross findings are shown in table VI. There is a steep rise with advancing age in the number of arteries affected. 8 cases in the under-40s had no calcification in any artery, but there was only 1 such case in the two older age-groups. The total number of arteries affected rose from 35 of the 75 vessels in the under-40s to 58 in the 50–59 age-group. The anterior descending artery was the one most frequently calcified in all the age-groups. The relationship of calcification to occlusion and stenosis is analysed in table VII. The occluded and the severely stenosed arteries show approximately equal frequencies of calcification, but the less severely stenosed vessels are less often calcified. The effect of age is again evident.

Heart-weight, Myocardial Scars, and Infarcts

In the absence of blood-pressure readings the only indication as to the frequency of hypertension comes from the heart-weights. These, together with the frequency and distribution of myocardial scars and infarcts, are shown in table VIII. The hearts have been divided into 4 groups, somewhat arbitrarily, assuming that those under 390 g. are normal, those of 390–420 g. are probably normal, those of 430–480 g. show the increased weight which may result from coronary-artery disease or from hypertension, while in those over 480 g. the hypertrophy almost certainly results from hypertension. If this is accepted, then there were 2–3 hypertensive subjects in the youngest group, 4–7 in the 40–49 age-group, and 4–6 in the oldest group, giving a total of between 10 and 16 hypertensives in these 75 sudden-death victims.

TABLE VI—CALCIFICATION

Age-group (yr.)	No. of calcified arteries (cases)				Arteries calcified			
	Nil	1 art.	2 art.	3 art.	L.A.D.	C.	Rt.	Total
Under 40 ..	8	6	4	7	13	12	10	35
40–49 ..	1	7	7	10	24	14	14	52
50–59 ..	1	4	6	14	24	18	16	58
Total ..	10	17	17	31	61	44	40	145

The scars and infarcts are also listed in table VIII where the subdivision indicates the arterial distribution area in which the lesion had occurred. It is not surprising that in these cases of sudden death infarcts were present in only a few hearts. Scars were found much more often in the older subjects, but the few infarcts were found principally in the younger groups. Infarcts were most often in the distribution of the right artery, and scars in the region of the left anterior descending vessel. A scar or infarct was, without exception, accounted for by occlusion or severe stenosis in the corresponding vessel; but there were many arterial lesions which had not resulted in corresponding myocardial damage.

TABLE VII—RELATIONSHIP OF CALCIFICATION TO OCCLUSION AND STENOSIS

Age-group (yr.)	Recently occluded arteries		Arteries 1/2 or more		Arteries 1/4 or less	
	Calcified	Not calcified	Calcified	Not calcified	Calcified	Not calcified
Under 40 ..	11	10	8	21	16	9
40–49	15	1	7	19	26	7
50–59	8	3	20	8	31	5
Total	34 (71%)	14 (29%)	35 (42%)	48 (58%)	73 (78%)	21 (22%)

Intercoronary Anastomoses

Anastomoses between left and right coronary arteries are demonstrated by extension of the injection medium from the right artery into the left in the first X-ray picture.

TABLE VIII—HEART-WEIGHTS, MYOCARDIAL SCARS, AND INFARCTS

Age-group (yr.)	Heart-weights (no. of hearts)				Scars				Infarcts			
	Under 390 g.	390–420 g.	430–480 g.	Over 480 g.	L.A.D.	C.	Rt.	Total	L.A.D.	C.	Rt.	Total
Under 40	8	14	1	2	4	2	3	9	5	3	5	13
40–49	9	9	3	4	10	1	3	14	3	..	5	8
50–59	3	16	2	4	11	2	8	21	1	..	2	3
Totals	20	39	6	10	25	5	14	44	9	3	12	24

TABLE IX—DETAILS OF 9 CASES SHOWING LESS THAN 5 cm. OF CONFLUENT ATHEROSCLEROSIS

Case no.	Age (yr.)	Length of artery diseased (cm.)			Degree of stenosis			Recent thrombosis			Calcification			Heart-weight (g.)	Myocardial scar	Nutrition
		L.A.D.	C.	Rt.	L.A.D.	C.	Rt.	L.A.D.	C.	Rt.	L.A.D.	C.	Rt.			
1	33	1·5	—	—	1/4	—	—	Occlusive	—	—	—	—	—	390	L.A.D.	Normal
2	36	3	—	—	1/6	—	—	Mural	—	—	—	—	—	360	—	Spare
3	36	1·5	—	—	1/5	—	—	Occlusive	—	—	—	—	—	390	L.A.D. (*c*)	Stout
4	45	4	—	—	1/5	—	—	—(*a*)	—	—	+	—	—	510	L.A.D. (*c*)	,,
5	48	3	—	—	1/5	—	—	—	—	—	—	—	—	360	L.A.D.	Spare
6	49	—	—(*b*)	—	—	1/8	—	—	Occlusive	—	—	+	—	390	—	Normal
7	51	2·5	—	—(*b*)	1/5	—	1/10	Occlusive	—	—	—	—	—	420	Rt.	,,
8	52	4	—	—	1/10	—	—	—	—	—	+	—	—	390	—	,,
9	52	4	—	—	1/6	—	—	Mural	—	—	+	—	—	530	—	,,

(*a*) Recanalised old occlusion. (*b*) Scattered plaques only but stenosis at 3 cm. (*c*) Scar extended by fresh infarction.

This simplified technique may not reveal lesser anastomoses, but it seems probable that functional junctions between the two sides will be shown up. Of the 75 cases, 38 showed significant anastomoses. 8 of these were in the under-40 group, 13 in the 40–49 group, and 17 in the 50–59 group.

Discussion

In every case the crucial lesion in the coronary arteries was atherosclerosis, with or without recent thrombosis. This holds good both for the 9 who died with only a short segment of artery diseased, and for the more numerous cases in which confluent atherosclerosis affected 10 to 20 cm. of artery. We found nothing to support the suggestion of Gresham and Howard (1960a and b), on the basis of dietetic experiments on rats, that coronary thrombosis can occur in the absence of atherosclerotic plaques.

Morris (1951), comparing the prevalence of coronary atherosclerosis recorded in postmortem examinations at the London Hospital in 1908–13 with the records for 1944–49, showed that over this period there had been some reduction in the amount of mural atheroma in the population, but in spite of this there had been a tenfold increase in deaths from ischæmic heart-disease. In other words, Morris showed that there is no direct relationship between the amount of atherosclerosis in a population and the incidence of ischæmic heart-disease. Others have interpreted Morris's observations as implying that coronary thrombosis occurred apart from atheroma. This, however, is completely contrary to the facts as observed not only in this study but in the general experience of pathologists working with human material. Thrombosis is never seen without mural disease. The rare instances in which coronary occlusion may be due to syphilis, embolism, thromboangeitis, or dissecting aneurysm form such a small part of the great number of cases as to be insignificant.

The 9 men in our series who died with minimal extent of atherosclerosis can be regarded as the pathological counterpart of Morris's epidemiological observation—demonstrating the lack of direct correlation between extent of mural disease and occurrence of fatal occlusion of the lumen. These 9 cases are so distinctive that it is important to determine how they differ from the others (table IX). Their ages range from 32 to 52, with 3 cases in each age-group. Recent thrombus was present in 7 of them—rather more frequently than in the series as a whole—while calcification was less common. The left anterior descending artery was even more involved than in the series as a whole: in only 1 case was the local lesion in the circumflex artery; and 1 man (case 7) appeared to have survived an infarct from a circumscribed lesion in the right artery, only to succumb to a similar lesion in the left. 2 were probably hypertensive.

The only clear difference from the other cases lay in the short length of artery affected. If these cases could be recognised during life they might prove the most suitable for direct surgical intervention. It is important to realise that they can be found amongst patients in their fifties, as well as in the younger groups, for, according to a current impression, more localised disease occurs only in the younger subjects.

The frequency with which two or three of the arteries may be occluded or severely stenosed (table I) provides a gloomy prospect for coronary-artery surgery; for we must share the conclusion of Branwood and Montgomery (1956) that in most cases the failure of coronary circulation is due to lesions in many parts of the coronary tree. It seems that any technique for wide application would have to include provision for clearing at least two of the arteries, perhaps over several centimetres. Only just over half the arterial occlusions involved the left anterior descending artery; the right artery was occluded in over a third of the cases, and the circumflex in a fifth. Apparently the reputation of the anterior descending artery as the site of a much higher proportion of thrombotic occlusions is not merited. The anterior descending artery is, however, almost constantly stenosed in these cases: its lumen was reduced to one-third or less of normal in 73, and to one-quarter or less in 70, of the 75 hearts.

Comparison between age-groups, which was one of the prime purposes of this study, reveals few significant differences. The prevalence of multiple occlusions and stenoses is the same throughout. Recent occlusions are somewhat more frequent in the younger subjects, old organised occlusions in the later age-groups; and the degree of preocclusive stenosis is severe at all ages. The extent of confluent atherosclerosis is only slightly greater in the older groups but, as anticipated, more of their arteries are calcified. Though the heart increases in weight with age, the number of definitely hypertensive subjects is only slightly greater. Differences between the age-groups are slight and quantitative, with a gradation from the youngest to the oldest. There is nothing to support the contention that under the age of 40 fatal coronary disease differs in any essential way from the disease in older subjects.

Summary

The pathological features in hearts of 75 men who died suddenly from ischæmic heart-disease were compared by age-groups. There were 25 subjects in each of the age-groups: 20–39 years, 40–49 years, and 50–59 years.

The coronary arteries were studied by postmortem angiography, and microscopy of semiserial sections of the stenosed segments.

In every instance the arterial lesion was atherosclerosis, with or without thrombosis. Occlusive thrombosis was

observed only when pre-existing atherosclerosis had narrowed the lumen to one-third or less of its normal calibre.

Prevalence of occlusion and stenosis, extent and distribution of disease, calcification, and other features showed only slight graded quantitative differences between the age-groups. The disease in the young did not differ essentially from that in the older age-groups.

In 9 of the 75 cases occurring throughout the age-range the disease was remarkably localised, with less than 5 cm. of artery affected by confluent atherosclerosis. Stenosis and occlusion were nevertheless due to severe (though localised) atherosclerosis. This group would appear to offer the best prospects for coronary surgery.

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ANTIBIOTICS AND THE COMMON COLD

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Ritchie (1958a) suggested that attacks of the common cold are aggravated by bacteria, normally present in the nasopharynx, which invade the tissues during the course of the virus infection. He reported successful clinical trials, which supported this hypothesis, using either autogenous vaccines or small doses of antibiotics (Ritchie 1958b) at the beginning of the attack to prevent the secondary invasion by bacteria.

The small trial reported here had two objects. The first was to see if measures to subdue the severity of the common cold prevented exacerbations of bronchitis in subjects with pneumoconiosis, who often assert that an attack of bronchitis succeeds a head cold. The second was to confirm and to extend Ritchie's results in normal subjects. For these purposes two groups were studied: (a) men employed in a light engineering factory in South Wales, all except 1 of whom had pneumoconiosis, and the majority of whom had the history and symptoms of bronchitis (Higgins et al. 1956); and (b) normal subjects from this unit.

Methods

A specimen of saliva was collected from each volunteer, and the sensitivity of its flora to tetracycline, oxytetracycline, and chlortetracycline determined.

A simple technique was used: the drugs in the form of tablets (' Sentest ', 10 μg. per tablet) were laid on the surface of the culture plate and sensitivity was measured by the size of the zone of inhibition round the tablet. As was expected when using related drugs, the flora tended to be sensitive to or resistant to all three; but it often happened that in one of the sensitivity tests a few stray colonies grew within an otherwise clear zone of inhibition. The bacteriological report included these scanty but somewhat resistant colonies, and thus perhaps exaggerated the differences between the related drugs.

Active or dummy lozenges were allocated at random to subjects in the trial. A subject receiving active treatment, however, had the antibiotic to which his flora appeared fully sensitive; when more than one drug would have been suitable, the choice was again made at random.

The volunteers in the factory were asked to report to the sister in charge of the first-aid room at the first symptoms of a cold. Each was then given a box of nine of the lozenges already assigned to him, and told to suck one slowly 3 times daily for three days. Each of the active lozenges contained 15 mg. of the antibiotic. In Ritchie's original trial (1958b), two tablets a day were given for two days but in some cases this was later increased to two tablets a day for three days. Thus our dose of three lozenges daily for three days was considerably more than his. The change was made because we thought that the increased dose might be necessary in chronic bronchitics to inhibit acute exacerbations.

The assessment of results was based on Ritchie's hypothesis that symptoms of a cold are, during the first few days, due to the virus itself and that, after this, secondary bacterial infection is responsible. Therefore the subject reported to the first-aid room on the fourth day and told the sister whether his cold had gone, was better but not gone, or was unchanged. In the analysis the main criterion of success was taken as the disappearance of the cold after three days rather than its improvement.

The same procedure was adopted in the trial on the volunteers from the unit, but the effect of the lozenges was assessed by a medical member of the staff.

As both the sufferer and the assessor could be biased by their faith in the efficacy of the lozenges, particular care was taken to ensure that neither could discover for certain which ones had been issued. The three antibiotics were of different appearance, and dummy lozenges resembling tetracycline and oxytetracycline only were available, there being none like the yellow chlortetracycline lozenges. Therefore, instead of attempting to conceal the fact that different treatments were being used, we exaggerated the apparent number of treatments, using twelve different identifying numbers on the drug boxes. Two different numbers were used for each of the three active drugs, and three for each of the two dummies, the allocation being made at random. We are satisfied that, in fact, no subject did succeed in identifying his own lozenges, even by comparing boxes with his colleagues. We emphasise the care which was taken to achieve the " double-blind " principle, because in the assessment of relatively minor disorders such as the common cold subjective elements may play a large part.

Results

Tables I and II show the number of subjects in each sensitivity and treatment group and also the numbers of subjects reporting colds.

Among the factory subjects there were 28 first colds in the active group and 22 in the control group, 36% of the volun-

TABLE I—SENSITIVITY AND ALLOCATION TO DRUGS (FACTORY GROUP)

Sensitive to	Allocated to					Number reporting colds
	T	O	C	D	Total	
T	5	..	..	2	7	2
O	..	4	..	4	8	1
C	..	..	10	6	16	6
T.O	..	..	..	2	2	..
T.C	1	..	..	2	3	1
O.C	..	12	13	19	44	19
T.O.C	5	4	5	20	34	13
None	4	3	4	13	24	8
Total	15	23	32	68	138	
Number reporting colds	5	8	15	22	..	50
Number, excluding those insensitive	4	7	12	19	..	42

T = Tetracycline. C = Chlortetracycline.
O = Oxytetracycline. D = Dummy.

TABLE II—SENSITIVITY AND ALLOCATION TO DRUGS (UNIT GROUP)

Sensitive to	Allocated to					Number reporting colds
	T	O	C	D	Total	
T	1	..	..	..	1	1
O	..	2	..	1	3	2
C	..	..	4	1	5	3
T.O	1	..	..	..	1	..
T.C	..	..	..	2	2	1
O.C	..	8	7	15	30	15
T.O.C	2	..	2	4	8	7
None	1	..	1	3	5	4
Total	5	10	14	26	55	
Number reporting colds	3	5	7	18	..	33
Number, excluding those insensitive	2	5	6	16	..	29

teers reporting at least one cold. Among the unit subjects the division was more equal—15 active and 18 controls among the 60% reporting colds. The difference in the incidence of colds in the two groups may in part be explained by differences in their age-distribution, the unit subjects ranging from 15 to 69 with a mean age of 38, and the factory subjects from 38 to 73 with a mean age of 56·7 years. Lidwell and Sommerville (1951) have shown that the incidence of colds falls with increasing age.

Table III shows the effect of treatment on the first colds experienced in the two groups.

The numbers treated by the different active lozenges are too small to warrant separate analysis and the results were considered under the two headings of "active" and "dummy"

TABLE III—EFFECT OF TREATMENT ON FIRST COLDS

Group	Treatment	Cured in 3 days	Improved in 3 days	No effect	Total
Factory	Dummy	5 (3)	9	5	19 (3)
	Tetracycline	3 (1)	1	..	4 (1)
	Oxytetracycline	4	2	1 (1)	7 (1)
	Chlortetracycline	4 (2)	7 (1)	1	12 (3)
Unit	Dummy	3	7	6 (2)	16 (2)
	Tetracycline	..	1	1 (1)	2 (1)
	Oxytetracycline	2	1	2	5
	Chlortetracycline	5 (1)	..	1	6 (1)

Figures in parentheses are the additional cases with insensitive organisms at the beginning of the trial.

treatments, a justifiable step as the drugs are chemically related (table IV). The cases apparently insensitive to all three antibiotics are shown in parentheses and are omitted from the following analysis.

In the factory group 26·3% of those on dummy lozenges and 47·8% of those on active lozenges were cured in three days; in the unit group, the figures were 18·8% and 53·8% respectively. The proportions cured or improved in three days differed less between dummy and active treatment: 73·7% and 91·3% respectively in the factory group, 62·5% and 69·2% in the unit group. As has been mentioned, the proportion of colds cured in three days is a better index of the validity of Ritchie's hypothesis; and, therefore, those merely improved in three days are best included in the "no effect" group. On this basis, the difference in the proportions cured on active and dummy

TABLE IV—COMPARISON OF ACTIVE AND DUMMY TREATMENTS ON FIRST COLDS

Group	Treatment	Cured in 3 days	Improved in 3 days	No effect	Total
Factory	Dummy	5 (3)	9	5	19 (3)
	Active	11 (3)	10 (1)	2 (1)	23 (5)
	Total	16 (6)	19 (1)	7 (1)	42 (8)
Unit	Dummy	3	7	6 (2)	16 (2)
	Active	7 (1)	2	4 (1)	13 (2)
	Total	10 (1)	9	10 (3)	29 (4)

Figures in parentheses are the additional cases with insensitive organisms at the beginning of the trial.

treatment attains the 20·8% level of significance in the factory group and the 6·5% level in the unit group.

The proportions cured in three days in both groups on active treatment (47·8% and 53·8%) are similar; so are the proportions cured on dummy treatment (26·3% and 18·8%). The data may, therefore, be combined and this has been done by adding the excess of cases cured in three days by active over dummy treatment in each group. Table IV shows that if there were no effect of treatment one would expect $16 \times {}^{23}/_{48}$ or 8·76 cases to be cured by active tablets in the factory group. The excess, 11 − 8·76 or 2·24 cases, is shown in table V, together with the corresponding excess of 2·52 cases in the unit group. The total excess, 4·76 cases, has a standard error of 2·02 and thus differs from zero at the 2% level of significance. The best estimate of the proportion cured with active lozenges in three days, a weighted average of 48% in the factory and 54% in the unit, is 50% with a standard error of ±8·3%. Since 22·9% of the colds were also cured in three days on dummy lozenges, the additional cure-rate of active tablets amounts to 35·2±12·3%.

TABLE V—EXCESS OF CASES CURED BY ACTIVE OVER DUMMY TREATMENT

Group	Excess of cases cured in 3 days	Variance
Factory	2·2381	2·4537
Unit	2·5172	1·6204
Total	4·7553±2·0184	

In addition to these results, there were 19 subjects whose first-reported colds started in the chest. They were given the same treatment regimen as those already considered, and table VI shows that 6 of them were cured in three days: the proportion is so similar in both treated and control groups that there is no evidence of any difference between them.

As reports of second and subsequent colds might have been influenced by the subject's initial experience, their cure-rates were not used to modify the estimates obtained from the first colds. Although the numbers of people with multiple colds are small, interestingly there appears to be an excess of persons who are either always or never cured, and a deficiency of persons who are sometimes cured (table VII). A similar effect is shown by the cure-rates of second and subsequent colds, divided according to whether the first cold was cured or not. None of these

TABLE VI—CHEST COLDS (FACTORY GROUP)

Treatment	Cured in 3 days	Improved in 3 days	No effect	Total
Dummy	4	6 (1)	2	12 (1)
Active	2	4	1	7
Total	6	10 (1)	3	19 (1)

Figures in parentheses are the cases with insensitive organisms at beginning of trial.

differences is, of course, statistically significant, but all suggest that there may be a tendency for successive colds attacking the same subject to behave similarly. Thomson and Glazebrook (1942) found some evidence to support this when investigating infectious disease in a semiclosed community.

The trial ended in the spring of 1959; and, in the autumn, a sample of saliva of as many as possible of the volunteers was re-examined. There appeared to be many more whose flora showed some resistance, but it was not clear how much the treatment had been responsible for this because the change was also found among those who had had dummy tablets. In those in whom the organisms had become insensitive, the insensitivity was to all three antibiotics. It is possible that there had been a spread of

TABLE VII—SUBJECTS HAVING MULTIPLE COLDS

—	Observed	Expected
Subjects always or never cured	13	9·5
Subjects sometimes cured	8	11·5

drug-resistant flora in the two communities, but it is also possible that there had been a seasonal change. Tables VIII and IX show the details.

The factory sickness-record was analysed during the seven months of the trial, and showed that 13 of the 28 men who took active lozenges for head colds and 9 of the 22 who took dummy lozenges were absent for over a week with diseases of the respiratory tract. The average number of spells per man were 0·61 and 0·64 respectively. In only one case, however, did an attack of bronchitis, necessitating absence from work, definitely follow a head cold. Most of the other periods of absence were due to illnesses described as starting in the chest.

Discussion

Ritchie's (1958a and b) hypothesis of the natural history of the common cold and the effect on it of oral antibiotics is well supported by our studies, the number of colds cured in three days being significantly higher after active treatment. Further, one would not expect oral antibiotics to affect the course of colds beginning in the chest if the enhanced activity of the subject's bacterial flora is assumed to have already begun at the time of onset. The negative results in the group of chest colds may therefore provide more support for the hypothesis.

TABLE VIII—CHANGE IN SENSITIVITY OF SALIVARY ORGANISMS DURING THE TRIAL (FACTORY GROUP)

—	Treatment				
	Chlor-tetra-cycline	Oxy-tetra-cycline	Tetra-cycline	Total active	Dummy
Becoming insensitive ..	4	4	1	9	9
Becoming sensitive ..	.. (*1*)	..	..	.. (*1*)	.. (*2*)
No change	6	6 (*1*)	4	16 (*1*)	16 (*2*)
Not re-examined ..	4 (*2*)	1	0 (*1*)	5 (*3*)	6

Figures in parentheses are the additional cases with insensitive organisms at the beginning of the trial.

Numbers are too small to infer whether any particular antibiotics are more effective than others in speeding the cure of head colds, or to assess the advantages gained from allocating subjects according to the sensitivity of their salivary organisms. The apparent increase in the number of subjects after the trial whose saliva contained insensitive organisms suggests the need for extensive investigation on the development of drug-resistant organisms before the widespread use of antibiotics could be recommended for the common cold.

TABLE IX—CHANGE IN SENSITIVITY OF SALIVARY ORGANISMS DURING THE TRIAL (UNIT GROUP)

—	Treatment				
	Chlor-tetra-cycline	Oxy-tetra-cycline	Tetra-cycline	Total active	Dummy
Becoming insensitive ..	3	2	0	5	3
Becoming sensitive ..	..	..	..	..	.. (*1*)
No change	3	3	2	8	11 (*1*)
Not re-examined ..	0 (*1*)	0	0 (*1*)	0 (*2*)	2

Figures in parentheses are the additional cases with insensitive organisms at the beginning of the trial.

From this trial we cannot decide the optimal dosage.

There were 9 subjects in all who complained either of soreness of the tongue or of the throat which usually began the day after the course of lozenges had been completed. This soreness in all but 3 was slight but tended to persist for several days. 6 of the cases occurred among the 24 subjects who took chlortetracycline and these included the 3 severer cases; 3 occurred among the 17 who took oxytetracycline. There were no symptoms in the 8 taking tetracycline, or in those taking the dummy lozenges. Ritchie (1958b) mentions the same problem and suggests that vitamins should be taken with the tablets.

In future trials the effects of smaller doses should perhaps be investigated, as also should the use of penicillin.

Summary

Ritchie (1958a and b) has suggested that small doses of antibiotics taken at the beginning of the common cold can prevent a secondary bacterial invasion and therefore shorten the duration of symptoms. The present trial was designed (a) to test whether these measures could prevent exacerbations of bronchitis in subjects with pneumoconiosis, and (b) to confirm and extend Ritchie's findings in normal subjects.

Two groups of subjects were studied: 138 ex-miners with pneumoconiosis and some degree of bronchitis, and 55 normal adults of both sexes.

Either dummy lozenges or ones containing 15 mg. of tetracycline, oxytetracycline, or chlortetracycline (depending on the sensitivity of the salivary organisms) were given at the earliest symptoms of a cold, the allocation to active or dummy lozenges being at random. The dose was 3 lozenges daily for three days.

The proportion of all first colds cured in three days on active lozenges in the bronchitic subjects and in the normals was similar; the two groups on dummy lozenges also behaved similarly. In the groups combined, about 23% of colds were cured in three days on dummy lozenges and this was significantly increased to 50% in those taking active lozenges, thus confirming Ritchie's hypothesis.

There was no evidence that the antibiotics speeded the cure of colds starting in the chest. There was no appreciable reduction in the number of spells of absence due to illness among those ex-miners taking the active lozenges, but this may be because only one severe exacerbation of bronchitis followed a head cold.

After the trial, more subjects had resistant salivary organisms; but they were found about equally in those taking active and dummy lozenges, and their significance is uncertain.

The weight of evidence now strongly supports the idea that recovery from the common cold can be speeded by treatment with antibiotics. The most suitable antibiotic and the optimal dosage have not yet been determined.

We are grateful to Dr. J. C. Gilson, director of the unit, for much help in planning the trial; and to Dr. I. T. T. Higgins and the factory sister for assessing the colds. We are indebted also to the factory management and to the factory medical officer for facilities afforded; and to all the subjects who took part for their ready cooperation. Lastly, we thank Messrs. Lederle for supplies of 'Achromycin' and 'Aureomycin' lozenges, and Messrs. Pfizer for supplies of terramycin.

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TELEVISION-INDUCED SEIZURES

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MANY varieties of sensory, intellectual, and emotional stimuli seem capable of provoking seizures in specifically sensitive people (Symonds 1959). Those most commonly effective are visual, and of these the best known is the flickering light. Epilepsy resulting from flicker has been reported under widely different circumstances, e.g., blinking, waving the abducted fingers in front of the eyes while facing bright sunlight (Bickford et al. 1953, Robertson 1954, Hutchison et al. 1958, Whitty 1960), driving down a tree-lined road against a setting sun (Cobb 1947), or simply walking along reflecting railings.

The complexities of modern life have introduced many new forms of flicker—e.g., neon and fluorescent lighting, and the cinema and television—but the number of people in whom seizures have resulted is surprisingly small. We have recently had two patients in whom epileptic fits were provoked by close proximity of the face to a flickering television screen. Investigation revealed some possible reasons for the rarity of the disorder.

Case-reports

Case 1.—A healthy housewife, aged 42, was a regular television viewer. There was no past history of head injury or encephalitis, and no family history of epilepsy. Discoid lupus erythematosus had been diagnosed 9 years previously, and for this she had been taking chloroquine phosphate (400 mg. daily) for several weeks.

In January, 1960, the family acquired a new large-screen television set, which failed to function properly. The screen was intensely illuminated, and " thick black bars passed from top to bottom ". The patient knelt beside the set to manipulate the controls, her face within six inches of the screen. She remembers manipulating the switches and feeling intensely distressed, and then she abruptly lost consciousness. Her husband witnessed a major epileptic seizure.

She was admitted to Hammersmith Hospital for investigation in March. There had been no further episodes. General and neurological examinations were entirely normal.

The blood-count, urine, cerebrospinal-fluid pressure and composition, and skull radiographs were normal, and the Wassermann reaction was negative.

Electroencephalography

Five baseline tracings were all normal, containing a regular symmetrical alpha rhythm at 8 c.p.s., which was readily blocked by opening the eyes or by any attention-provoking stimulus, including visual imagery. Overbreathing for 3 minutes repeatedly failed to alter the tracing.

Photic stimulation from a flickering source (Xenon-discharge tube, E.M.I. model 3c) at frequencies of 18–30 f.p.s. immediately produced fast regular symmetrical and synchronous spikes (fig. 1), followed by myoclonic jerking. The myoclonus proceeded to a major convulsion if allowed to continue for more than a few seconds.

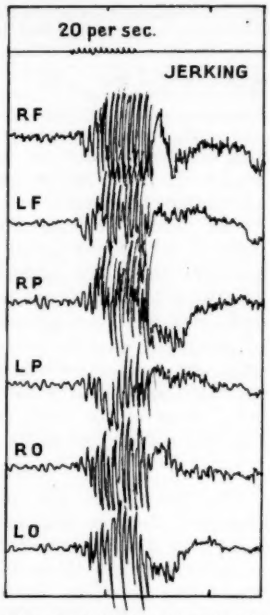

Fig. 1—Multiple spikes in all regions induced by flicker at 20 f.p.s.
Distance 8 inches. Eyes closed.
F = frontal ; P = parietal ; O = occipital.

Photic stimulation in the ranges 3–18 f.p.s. and 30–40 f.p.s. produced various combinations of generalised paroxysmal slow waves, spike-and-wave, and polyspike-and-wave complexes (fig. 2). At these flash frequencies rhythmic spike activity (and

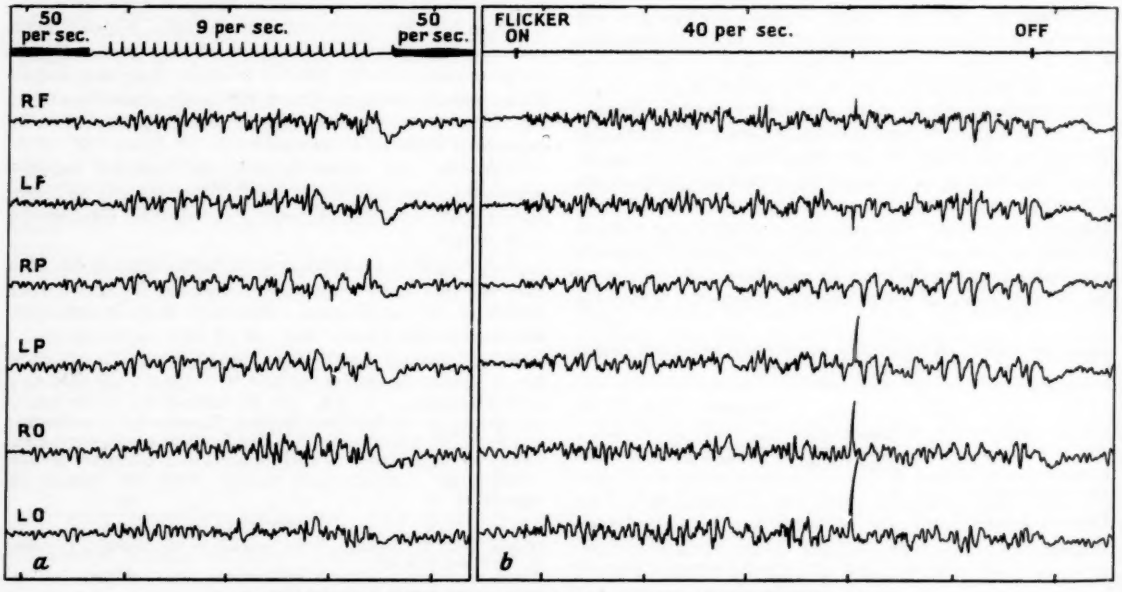

Fig. 2—Spikes and slow waves induced by flicker at (*a*) 9 f.p.s., and (*b*) 40 f.p.s.
No response at 50 f.p.s. Distance 14 inches. Eyes closed.

clinical myoclonus) took somewhat longer to develop than at 18–30 f.p.s. No electrical or clinical disturbance could be produced at flash frequencies of 50 f.p.s. (fig. 2*a*).

At the optimum epileptogenic frequency of 20 f.p.s. spikes and myoclonus were provoked when the source of light was held within 45 in. of the patient's eyes.

At all distances within the effective range, and at all frequencies between 3 and 40 f.p.s., both spikes and myoclonus could be produced with greater ease and earlier when the eyes were closed than when they were open.

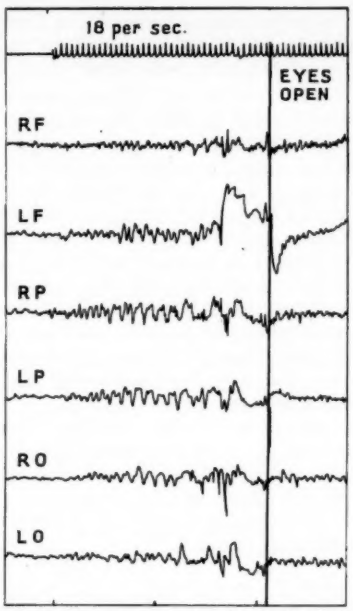

Fig. 3—Slow waves and spikes induced by flicker at 18 f.p.s. and abolished by opening the eyes.
Distance 40 inches.

At a distance of 40 in. and at a flicker frequency of 18 f.p.s., the spikes and slow waves produced when the eyes were closed could be abolished by opening the eyes (fig. 3). They would return when the eyes were again closed. Mental arithmetic and visual imagery failed to inhibit the spikes.

At all distances and flash frequencies the contrast between background illumination and intensity of the flicker source seemed significant. In a darkened room both the spikes and their clinical concommitants were easier to produce. When the stimulus was applied against a brighter background a longer exposure was required to produce spikes and jerking.

The susceptibility to all the parameters of stimulation was extremely constant from day to day, and at various times within a given day.

Case 2.—An indoor decorator and regular television viewer, aged 27, suddenly lost consciousness at work in March, 1960. The onset of the episode was not witnessed. He was not incontinent and did not bite his tongue or sustain any injury, but he remained " unconscious " for 2 hours. In July, while adjusting a defective television set, he knelt with his face near the flickering screen. He felt giddy, and then suddenly lost consciousness. His wife witnessed a typical major epileptic seizure. The past and family histories were non-contributory.

General and neurological examinations were entirely normal. The blood-count, erythrocyte-sedimentation rate, cerebrospinal-fluid pressure and composition, and radiographs of skull and chest were normal, and the Wassermann reaction was negative.

Electroencephalography

The resting records were abnormal. The alpha rhythm was symmetrical, regular, and of moderate amplitude, it blocked on opening the eyes and during other attention-provoking stimuli. It was interrupted by occasional paroxysmal bursts of symmetrical synchronous large-amplitude theta and delta waves, associated with irregular spikes and sharp waves. Overbreathing caused an increase in the amount of paroxysmal activity.

Photic stimulation at frequencies of 9–30 f.p.s. constantly gave rise to paroxysmal abnormalities. These varied from bursts of multiple symmetrical synchronous fast spikes at flash frequencies of 11–21 f.p.s. to bursts of irregular spike-and-wave and polyspike-and-wave complexes (22–30 f.p.s.). Generalised myoclonic jerking began when spike activity was allowed to continue for more than a few seconds. No abnormalities could be produced at flash frequencies of 50 f.p.s.

To elicit a response the flicker source had to be within 35 inches of the patient's eyes. Paroxysmal responses to flicker were always produced more readily with the eyes closed than with the eyes open.

The range of flicker frequencies required to produce given patterns of paroxysmal electrical abnormalities remained constant throughout the period of observation, but the other parameters of effective stimulation (distance and contrast) varied somewhat from day to day.

Discussion

The incidence of clinically manifest epilepsy in the general population is high (5 per 1000 in Holland, Switzerland, and America according to Brain [1955]). Latent susceptibility must be even more common. Yet, despite the widespread exposure of such susceptible individuals to television flicker, the incidence of " television-induced seizures " is very low. Some cases of television epilepsy may go unrecognised, but the number recorded is clearly less than might be expected. We have only been able to discover two cases in the English journals (Klapetek 1959, Whitty 1960); these patients also had spontaneous attacks. A further dozen or so patients have been seen at The National Hospital, Queen Square (Dr. W. A. Cobb, personal communication), who have had seizures while watching television. Like our second case all were young patients, and some had also had spontaneous seizures.

The discrepancy between the rarity of television epilepsy and the frequency with which susceptible people are submitted to potentially effective stimuli may be explained by some of our observations. The highly specific nature of the effective stimulus is borne out by the clinical data. The only time these habitual televiewers had seizures induced by flicker was when their eyes were in close proximity to a brilliantly illuminated and relatively slowly flickering screen in a darkened room. Both patients then experienced distress, probably closed their eyes, and lost consciousness. Electroencephalographically the effective stimulus was highly specific. For example, in the first case (1) the flicker frequency had to be between 3 and 40 f.p.s., and preferably 18–30 f.p.s.; (2) the flicker had to be applied within a distance of 45 inches, in other words apparent brightness appeared to be an important factor; (3) the degree of contrast between the light flashes and the environmental illumination appeared to be significant, conforming with previous observations (Toman 1941) on " photic driving "; and (4) an increased responsiveness to flicker was demonstrated when the eyes were closed.

This increased susceptibility to flicker when the eyes are closed has been noted by Bickford et al. (1953) and Robertson (1954) in describing children with self-induced photogenic epilepsy. The mechanism of this remains obscure, but at least two possibilities should be considered:

One is that the eyelid acts as a differential light filter, but what evidence there is does not support this contention. Bickford et al. (1953), using coloured filters, found that " the convulsive effect of light is not confined to any small segment of the visible spectrum and seizures may be produced with pure red, green or blue light ", and they concluded " that all parts of the visible spectrum contribute to the effect ".

The variation in susceptibility to flicker (according to whether the eyes are open or closed) might alternatively be related in some way to the blocking of the alpha rhythm

with attention-provoking stimuli. In both our patients opening the eyes diminished the flicker-induced spikes and abolished the alpha rhythm. Other attention-provoking stimuli (such as visual imagery, calculation, and noise) abolished the alpha rhythm but had no specific effect on the flicker-induced abnormalities. These observations may be explained by the fact that eye opening may be the most potent of all attention-provoking stimuli, but might also imply the operation of two separate mechanisms, one for " alpha-blocking " and the other for " spike-blocking ".

Our first patient showed an exquisite sensitivity to flicker despite a normal resting record. This is most unusual in epilepsy precipitated by visual stimuli, but it has been previously reported (Bickford et al. 1953, case 23; Robertson 1954, cases 3 and 7; and Hutchison et al. 1958, case 2). Our patient seems to be unique in that her one and only attack was at the age of 42, in response to flicker. All previously reported cases were known epileptics who were liable to spontaneous seizures as well.

With regard to prevention of future attacks, two points might be emphasised. As far as possible susceptible persons should avoid bringing the face near a slowly flickering screen in a darkened room. Should this be impossible, however, and should distress be experienced during the procedure, patients should be instructed to turn promptly away, and under no circumstances to remain facing the screen with their eyes closed.

Summary

In two unusual cases of epilepsy the patients had attacks while watching television. In both the parameters of effective photic stimulation were highly specific. This may account for the rarity of this condition although potentially susceptible people are often exposed to television flicker.

We are grateful to Dr. Cobb, of The National Hospital, Queen Square, for helpful advice and criticism, and to Miss A. M. Lees for the E.E.G. recordings.

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EPILEPSY AND TELEVISION

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Apuleius, a Roman contemporary of Galen, mentions in his Apologia that a seizure might be provoked when a potter's wheel was rotated before the eyes of a slave (Temkin 1945). This ancient slave-dealers' test for epilepsy is probably the earliest recorded association of fits with flickering light. Among modern physicians, Gowers (1881) was the first to recognise that light might precipitate epilepsy.

Clinical observations of the effects of light have been augmented by electroencephalographic (E.E.G.) investigations. Adrian and Matthews (1934) showed that rhythmic changes in electrical potential could be recorded over the occiput when a subject's eyes were exposed to bright flickering light. Walter et al. (1946) evoked spike-and-wave discharges in an epileptic by photic stimulation. Many workers (Cobb 1947, Gastaut et al. 1948, Walter and Walter 1949) have confirmed the existence of a group of epileptics who are sensitive to light, and particularly to flickering light. Fits of all clinical types have been precipitated by photic stimulation. Some epileptics have discovered how to use light to induce fits in themselves (Hutchison et al. 1958, Whitty 1960).

In recent years a television screen (usually one which is flickering) has sometimes provoked fits in susceptible people. Such cases have been described by Livingston (1952), Klapetek (1959), and Whitty (1960). All these patients, however, had fits on other occasions, and it was not always possible to produce E.E.G. abnormalities on photic stimulation with the stroboscope. Dalby (1958) described two children who had major convulsions whilst watching television, and in both of these photic stimulation evoked abnormalities in the E.E.G. as well as inducing fits. One child had previously had five fits following minor head injuries.

The three patients described below are of interest because of the striking association between their convulsions and watching television, and because recognition of this association was helpful in their management. None of them had a family history of epilepsy, and no abnormal signs were found.

Case-reports

Case 1.—A woman, aged 34, was seen in February, 1959. For 5 years she had had occasional attacks of migraine, sometimes precipitated by the glare of bright sunshine. 2 months previously she was watching television when the picture disappeared and the screen flickered. She bent down to adjust the controls, lost consciousness, and had a grand-mal convulsion. She again had a similar fit 5 days before being seen, also while she was adjusting the controls of the television set because the screen was flickering.

The E.E.G. showed a normal resting record with a sustained alpha rhythm of 9-13 c.p.s. Overbreathing elicited no abnormal features. Photic stimulation with the eyes closed produced no significant change, but with the eyes open and a flicker frequency of 12 f.p.s., spike and slow-wave complexes appeared in all areas. At frequencies of 18-20 f.p.s. these complexes reached their highest peak. Stimulation at these frequencies was prolonged for 5 minutes but the E.E.G. pattern did not change further, nor did the patient's clinical condition.

Case 2.—A girl, aged 16, was first seen in December, 1959. 3 months before, when watching television for the first time, the screen flickered and she bent down to adjust the controls. She then had a grand-mal fit.

The E.E.G. showed a resting record with a well sustained alpha rhythm at 9-11 c.p.s. and scattered low to medium voltage slow waves at 2·5-3·5 c.p.s. in central and posterior leads. After overbreathing for 25 seconds there was a short widespread discharge of high-voltage slow activity at 2-3 c.p.s. Photic stimulation with the eyes closed produced no significant change; with the eyes open and at frequencies of 15-30 f.p.s. high-voltage atypical spike-and-wave discharges were elicited. These discharges were inhibited by closing the eyes and removing the stimulus. After 10 seconds' continuous stimulation at a frequency of 20 f.p.s. the patient had a grand-mal convulsion.

Case 3.—A girl, aged 16, was seen in June, 1959. A year before she was watching television when the picture disappeared and the screen flickered. She bent down to adjust the controls, felt dizzy, and then had a grand-mal attack. She had four further attacks at intervals of months—all when she was adjusting the controls of a flickering television set.

The E.E.G. showed a resting record with medium voltage alpha rhythm at 8-10 c.p.s. A background of low-voltage fast activity at 14-20 c.p.s. was present in all areas symmetrically. Low to medium voltage theta waves at 5-7 c.p.s. arose at random in all areas. Overbreathing augmented the resting rhythms, and, at intervals of 5-6 seconds, sharp and slow-wave complexes appeared, maximal in the postcentral areas. Photic stimulation with single flashes produced spikes, at the same

frequency as the flash-rate, in posterior leads only. When the flash-rate increased a grand-mal convulsion followed, accompanied by a general discharge of spikes and sharp waves.

Discussion

The histories of these patients are similar. In all three, fits were provoked on fairly prolonged and close exposure to a flickering television screen, as each watched whilst adjusting the controls. All showed striking E.E.G. changes, and two of them had fits when stimulated with the stroboscope. They described the flickering in similar terms; the picture disappeared from the screen and was succeeded by horizontal lines, alternately light and dark, which seemed to move downwards. They likened the appearance to that often seen when a set is " warming up ", before the picture has come into focus. This is probably due to a loss of synchronisation between the signal and the time base, which is likely to produce a flicker frequency of about 25 f.p.s.

Because of the consistent association of their fits with faulty reception on their television sets, these patients were advised to look away from the screen whenever it flickered. All three were given anticonvulsants, either primidone or phenobarbitone with sodium phenytoin. Periods of 9 months, 18 months, and 14 months respectively have elapsed since treatment was started, and none of these patients has had a further attack.

A television set, particularly one which is temporarily faulty, can provide a potent source of photic stimulation. Epileptics who are sensitive to light should avoid this precipitating factor.

Summary

Three cases are described in which epileptic fits were provoked only when watching a flickering television screen.

I wish to thank Dr. F. R. Ferguson, in whose clinic these patients were seen, for his advice, and for drawing my attention to case 1.

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CHANGES IN VENTILATORY FUNCTION AFTER ABDOMINAL OPERATIONS

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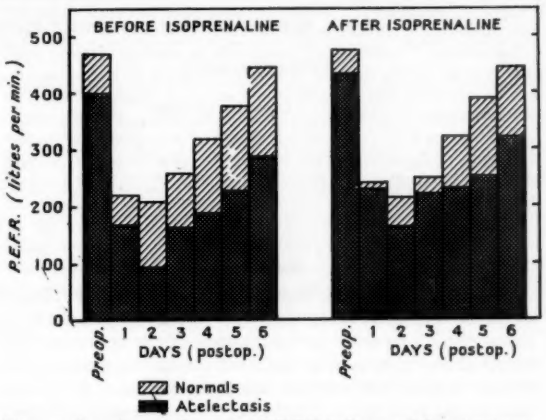
SINCE the clinical features of lobar atelectasis of the lungs were first described (Pasteur 1908, and 1910), much has been learnt about postoperative pulmonary complications. Yet, in spite of advances in anæsthesia, and the use of antibiotics and physiotherapy, these complications are still common after abdominal surgery. They are a source of worry to the surgeon and the anæsthetist, and of discomfort, and sometimes of danger, to the patient.

Postoperative atelectasis is most likely after upper abdominal operations in male patients especially those who have bronchitis, are heavy cigarette smokers, or have recently had an upper respiratory infection. Nevertheless, it is not always easy to predict either before, or immediately after, the operation which patient will have atelectasis;



Mean peak expiratory flow-rate (P.E.F.R.) after partial gastrectomy.

and, when massive lobar atelectasis does occur, those looking after the patient are often taken by surprise. It has been suggested that atelectasis takes place in patients who readily have bronchial spasm and who secrete a viscid bronchial mucus. The combination of bronchial spasm, viscid mucus, and the reduction in ventilatory capacity always seen after laparotomy leads to sputum retention and atelectasis, and often to bronchopneumonia (Palmer and Sellick 1953). Ventilatory capacity may be reduced to 20% of the preoperative figure after upper abdominal operations. These changes affect total lung capacity and its subdivisions (Anscombe and Buxton 1958). Using the maximum breathing capacity (M.B.C.), measured before and after the inhalation of a bronchodilator, an attempt was made to discover if there were abnormalities in ventilatory function in high-risk cases or in those which later had atelectasis. Whereas there was no significant increase in postoperative M.B.C. after the inhalation of a bronchodilator in patients with normal chests, 2 patients with bronchitis (1 of whom later had atelectasis) showed significant increases in M.B.C. after the bronchodilator (Palmer 1958). This suggested that high-risk cases and those whose lungs become ateletatic behave differently from normals after the operation.

In order to study these changes further, and in particular to detect the development of bronchial spasm, ventilatory function has been measured in patients undergoing abdominal surgery, preoperatively and postoperatively, before and after the inhalation of isoprenaline. These measurements were made with the Wright flowmeter, which is a sensitive portable apparatus for determining peak expiratory flow-rate (P.E.F.R.) in litres per minute (Wright and McKerrow 1959).

Method

39 patients were studied, all of whom had been admitted to a surgical unit for elective surgery for chronic peptic ulcer. There were 30 men and 9 women. Two readings of P.E.F.R. were made before, and two after, the inhalation through an ' Agla ' hand inhaler of 1 ml. of a 1% solution of isoprenaline (' Neo-Epinine solution no. 1 ', Burroughs Wellcome), before the operation, and for six days afterwards. Chest radiographs were taken routinely during the first two postoperative days, or more frequently if indicated clinically. Throughout the experiment the usual routine treatment for the prevention of atelectasis was given. This consisted of physiotherapy and assisted coughing.

MEAN INCREASE IN PEAK EXPIRATORY FLOW-RATE (LITRES PER MIN.) AFTER ISOPRENALINE

Patients with atelectasis							Normals						
Before operation	Days after operation						Before operation	Days after operation					
	1	2	3	4	5	6		1	2	3	4	5	6
+33·5 (−10– +105)*	+60·7 (+45– +127)*	+98·8 (+63– +230)*	+64·5 (+44– +195)*	+45·8 (+10– +112)*	+22·9 (−10– +123)*	+26·8 (−8– +147)*	+10·4 (−35– +45)*	+20·6 (−30– +38)*	+5·8 (−43– +25)*	−9·8 (−20 – +19)*	+3·2 (−5– +28)*	+8·3 (−10– +40)*	+5·2 (−13– +31)*

* Range.

Results

10 patients showed definite radiological and clinical evidence of atelectasis; this was often followed by or accompanied by fever and purulence of the sputum. The figure shows the mean of the daily P.E.F.R. in the group in which atelectasis developed and those in whom it did not, before and after the inhalation of the isoprenaline. There is a considerable reduction in ventilatory capacity in both groups after the operation, but the reduction is greater in those patients who later had atelectasis. When the mean of the daily P.E.F.R. after isoprenaline in the cases of atelectasis is compared with that of the normals, it can be seen that there were considerable increases in P.E.F.R. in the atelectasis group, especially during the first three post-operative days. The table shows the extent of this change which was greatest on the second postoperative day (mean increase in P.R.F.R. 98·8 litres per minute—range 63–230). After isoprenaline preoperatively or postoperatively, only slight and inconstant increases in P.E.F.R. took place in normals.

Discussion

This study shows that laparotomy has a profound effect on the ventilatory function of the lungs. This change is greatest on the second postoperative day, when the P.E.F.R. is reduced to less than half of the preoperative level. This change occurs even in those whose lungs do not become atelectatic.

Two differences can be seen, however, between the cases of atelectasis and the normal group: (1) those in whom atelectasis arose later showed in general a greater impairment of ventilatory function after the operation than the normals, the preoperative value for P.E.F.R. not being regained by the sixth postoperative day; and (2) the cases of atelectasis—unlike the normals—showed big increases in P.E.F.R. after isoprenaline during the first three postoperative days.

These findings confirm the suggestion that bronchial spasm, at the time when the ventilatory function is least, is an important factor in the development of atelectasis. Moreover, these changes are greatest during the first three postoperative days, when atelectasis is most likely to occur (Stringer 1947).

Congestion of the bronchial mucosa and spasm of the bronchial musculature both reduce bronchial calibre, and these changes are often also accompanied by increases in the amount and viscidity of the bronchial secretion. When there is congestion or spasm of the bronchi, very small amounts of secretion may produce bronchial occlusion and atelectasis.

Bronchial spasm may arise in the induction period during passage of an endotracheal tube; during the operation because of rough handling of the viscera and traction on the mesentery (de Takats et al. 1942); or after the operation if there is severe pain (Lucas 1950). Patients with bronchitis are especially liable to have bronchial spasm and to have an increased amount of more viscous bronchial secretion in the postoperative phase. Moreover, bronchitics are particularly sensitive to the effects of postanæsthetic carbon-dioxide retention, which is likely to occur when ventilatory function is much reduced. The presence of even a slight degree of bronchitis is the most important single factor which disposes the patient to the development of chest complications after operations. Smokers and elderly men are high-risk cases because they commonly have bronchitis.

In patients with bronchitis there is often a significant increase in P.E.F.R. after the bronchodilator. This change is of much greater importance in predicting the chance of the development of atelectasis than a low initial P.E.F.R. which does not increase after the bronchodilator. Daily postoperative estimations of P.E.F.R., before and after a bronchodilator, are even more important; for those patients who show increases in P.E.F.R. after isoprenaline, or a profound reduction of ventilatory function (compared with the preoperative P.E.F.R.), must be regarded as high-risk cases. When these changes are present, atelectasis exists or will soon develop and vigorous treatment must be undertaken immediately to overcome sputum retention and bronchial spasm. Treatment should consist of the inhalation of isoprenaline followed by postural drainage with vibratory and clapping percussion to the chest wall, for it has been shown that both are necessary for the prevention and treatment of postoperative atelectasis (Palmer and Sellick 1953). This study provides a rational explanation for the success of this regimen.

Summary

The peak-expiratory flow-rate (P.E.F.R.) has been used to study ventilatory function after abdominal operations.

Measurements were made preoperatively and post-operatively, before and after the inhalation of a broncho-dilator drug (isoprenaline), in patients undergoing elective surgery for chronic peptic ulceration. The measurements were made to determine whether changes in P.E.F.R. would help in picking out those patients liable to have post-operative pulmonary complications. It was found that patients in whom atelectasis later took place showed (1) greater impairment of ventilatory function after operation, and (2) larger increases in P.E.F.R. after the inhalation of isoprenaline during the first three postoperative days than did the normals. The significance of these findings in the prevention and treatment of postoperative pulmonary complications is discussed.

My thanks are due to Prof. W. C. Wilson, Mr. Hugh Dudley, and Mr. James Kyle for their cooperation and for allowing me to examine their patients.

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RELATION OF HYPERTENSION TO UNILATERAL RENAL ATROPHY

A Study of Necropsy Records

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IN the twenty-five years since Goldblatt showed that partial ischæmia of the kidney could produce hypertension in laboratory animals, many reports have suggested that similar mechanisms may operate in man. Most of these reports have been based on clinical cases in which high blood-pressure reverted to normal after removal of an ischæmic kidney. We have not been able to find any analysis of postmortem material, and this is perhaps not surprising. Besides the usual difficulties in deriving significant statistics from postmortem material (see Johnson 1958), hypertension and renal disease may instigate each other; and this might make the task of disentangling cause and effect almost impossible.

Renal ischæmia itself presents some difficulties in recognition post mortem. Stenosis or occlusion of the main vessels cannot be evaluated objectively from routine necropsy reports; for, apart from difficulties in grading them, observations and interpretations will have been biased according to the foreknowledge of the prosector as to whether or not there had been severe hypertension. But severe ischæmia will produce atrophy of the kidney, and we thought that a study of unilateral renal atrophy might uncover cases of ischæmia and at the same time exclude most cases of glomerulonephritis, senile atrophy, essential hypertension, and " malignant " hypertension, in which renal atrophy is almost always bilateral.

Material and Methods

We have sought to thread a way through the inherent difficulties by utilising only recorded data which are as free as possible from subjective error. These data, obtainable from all but a few of our necropsy records, were the patient's blood-pressures, the weight of the kidneys, the difference between the left one and the right, and the causes of any unilateral renal atrophy. The study was based on the records of 5000 consecutive necropsies at the Banting Institute, University of Toronto, excluding neonatal deaths.

Blood-pressure of Patients

In a study such as this it is imperative to categorise degrees of physiological or anatomical abnormalities, and it might be thought that with records of blood-pressure readings this would be easy. But the same pressure readings have a different significance in different individuals, and furthermore this large series of cases included some in which the previous history and the significance of the blood-pressure recorded during the stay in hospital were uncertain. Fortunately in the cases with the very high readings the clinicians concerned had nearly always recorded a useful history. It is hard to get agreement on what constitutes " malignant " hypertension. Other people's notations on eye-grounds are hard to assess, and blood-pressure recordings have no real value in distinguishing between severe essential hypertension and so-called " malignant " hypertension. We have used the morbid anatomist's approach and have limited the use of the term " malignant " hypertension to cases in which we found ateriolar necrosis in the kidneys and to 1 case in which necrosis was present in the arterioles of the adrenal cortex. This is not an expression of opinion as to whether " malignant " hypertension is a separate entity or part of the spectrum of severe hypertension, but merely a convenient arrangement to see whether significant differences emerged. The other categories were formulated empirically on recorded heights of blood-pressure, the highest readings being used when patients had labile pressures. The categories were as follows:

" *Malignant* " *hypertension:* ateriolar necrosis present.

Grade-3 hypertension: blood-pressure of 220/110 mm. Hg or over.

Grade-2 hypertension: diastolic pressure of 100 mm. Hg. or over, with a systolic pressure in the neighbourhood of 200 mm. Hg.

Lesser degrees of hypertension such as might have been termed grade 1 were ignored in this survey.

Weights of the Kidneys

All of our necropsy reports record the weight of each kidney. These weights have, of course, some limitations. They do not indicate the actual weight of renal tissue, because of uncertain factors such as the amount of pelvic fat and the contents of renal cysts. The figures did, however, fix accurately the upper limits of what the actual renal tissue might weigh.

Over the years covered by this survey all of the kidneys were seen by one of us (H. J. B.), who controlled the indexing. Any kidney deemed significantly smaller than its fellow (our criteria in the survey were that one kidney should be 120 g. or over, and the other 100 g. or under) was indexed under the cause of the atrophy. These causes were: (1) ischæmia from occlusion or stenosis of the main renal vessel, (2) multiple infarcts, (3) chronic pyelonephritis, (4) hydronephrosis, (5) hypoplasia, and (6) unknown.

Only 3 cases were listed in the last two groups, which were therefore ignored. We already had a card listing the cases of ischæmic atrophy. We extracted all the other cases of unilateral renal atrophy by going through all the cases of renal infarction, chronic pyelonephritis, and hydronephrosis. These cases acted both as controls to the group showing ischæmic atrophy and as subjects of study in their own right.

Results

The classification of the cases with unilateral renal atrophy is shown in table I. Of 106 cases the renal atrophy was due to stenosis of the main vessels in 11. In the remainder it was due to the other listed causes in fairly even distribution. In many of the cases of obstruction of the urinary tract the atrophy was due to pyelonephritis as well as obstruction; but, as far as possible, we determined the predominant cause of the atrophy by studying the microscopic sections.

Table I also shows the prevalence of hypertension in each group. To understand the significance of these figures we had to know the prevalence of malignant and

TABLE I—PREVALENCE OF HYPERTENSION IN 106 CASES OF UNILATERAL RENAL ATROPHY

Cause of renal atrophy	No. of cases	No. with " malignant " hypertension	No. with grade-3 hypertension	No. with grade-2 hypertension
Stenosis of main vessels	11	6 (54%)	5 (46%)	0
Chronic pyelonephritis	34	1	4 (11·8%)	4 (11·8%)
Obstruction of urinary tract	37	0	2 (5·4%)	7 (18·9%)
Multiple infarcts	24	0	0	8 (33%)

TABLE II—PREVALENCE OF HYPERTENSION IN 5000 NECROPSIES

—	"Malignant" hypertension	Grade-3 hypertension	Grade-2 hypertension	Grade-2 + grade 3 hypertension	All cases of hypertension
All 5000 necropsies (observed or estimated)	0·78%	3·4%*	5·2%*	8·6%*	9·38%*
372 cases chronic pyelonephritis	1	..	..	50 (13·4%)	..
300 cases obstruction of urinary tract	..	..	..	33 (11%)	..

* Calculated from a series of 2927 necropsies.

essential hypertension in our necropsy material as a whole, and also in all of our cases of chronic pyelonephritis and obstruction of the urinary tract with or without unilateral renal atrophy. The number of these cases of renal disease and the prevalence of hypertension among them are shown in table II. Owing to difficulties of definition and inadequate records, we had no way of knowing how many cases of stenosis of the renal vessels and of multiple infarcts there were in the 5000 necropsies. The overall prevalence of malignant and essential hypertension is also shown in table II. The prevalence of essential hypertension had to be calculated from a smaller series than the 5000, because of the labour of checking clinical histories. These figures might be considered as giving us a control group. In the overall necropsy population the prevalence of " malignant " hypertension, grade-3 hypertension, and grade-2 hypertension was 0·78%, 3·4%, and 5·2% respectively, making a total of 9·38%. This figure can be compared to the prevalence of hypertension in all cases of obstruction of the urinary tract (11%) and in all cases of chronic pyelonephritis (13·4%).

Turning to the cases of unilateral renal atrophy (table I), the most striking finding was in the cases of renal atrophy due to stenosis of the main vessels. All 11 cases were associated with either grade-3 or " malignant " hypertension, and 6 of the 11 with " malignant " hypertension. Of all the cases of " malignant " hypertension in the 5000 necropsies, 1 in 6 was associated with unilateral renal atrophy. In other words we found that 1 in 10 of our cases of unilateral renal atrophy had " malignant " hypertension. We do not of course claim that all cases of unilateral renal atrophy due to stenosis of the renal artery are associated with " malignant " or severe hypertension. It just happened that way in our series.

Statistical Significance of Findings

In evaluating our figures we have used " confidence " limits from charts calculated by Clopper and Pearson (1934).

Table III, section *A*, shows that in 0·78% of 5000 of our necropsies " malignant " hypertension was present. The possible limits of this control figure, using charts demanding 95% confidence, are 0–2%. The possible range of our cases in which " malignant " hypertension was associated with unilateral renal atrophy is 21–86%, and the increased prevalence is therefore highly significant.

On the other hand the apparent increased prevalence of essential hypertension and unilateral renal atrophy is rendered suspect by the approximation of the upper limits of the control figures to the lower limits of our findings (table III, section *B*).

We might, however, argue that if two separate causes of renal atrophy produce nearly significant increases in the prevalence of hypertension, this should be accepted as some evidence that renal atrophy and hypertension may be associated. This weighting of evidence is expressed mathematically in table III, section *C*, where the cases of chronic pyelonephritis and obstruction of the urinary tract are added together. With the larger sample the confidence interval contracts, and the result is that the increased prevalence of hypertension becomes significant. In this section we have used all three types of hypertension as control, stating their observed or calculated prevalence in 5000 necropsies.

The conclusions from these figures are: (1) there is an unequivocal increase in the prevalence of " malignant " hypertension in the case of unilateral renal atrophy due to stenosis of the renal artery; (2) essential hypertension has an increased prevalence in the cases with atrophy due to stenosis of the renal artery and multiple infarcts; (3) there is strong evidence that the other two causes of renal atrophy are also associated with an increased prevalence of hypertension.

Possibility of Extension

Our figures relate only to the necropsy population of our particular hospital over a particular time, and may not represent the necropsy population of another hospital or a live population. There is no a-priori reason, however, for thinking that necropsy figures from other centres would be very different. Clawson (1941) analysed 30,215 necropsies and found that 8·6% had had hypertension. This compares well with our figure of 9·38% (confidence limits 8–12%).

Causality

Mathematics confirms our impressions that there is an increased prevalence of hypertension in unilateral renal atrophy due to ischæmia, but mathematics deserts us when we come to determining cause and effect. We could put forward either of the two following hypotheses: (1) occlu-

TABLE III—CONFIDENCE LIMITS OF FIGURES OF PERCENTAGE PREVALENCE OF HYPERTENSION

Type of hypertension	Disease	No. of cases	Percentage with hypertension	Confidence limits (%)*
A—"Malignant":				
In cases of unilat. renal atrophy	Stenosis of renal art.	11	54	21–86
In 500 necropsies (control)..	..	5000	0·78	0–2
B—Essential:				
In cases of unilat. renal atrophy	Stenosis of renal art.	11	45·5	15–79
	Chr. pyelonephritis	34	24·7	10–44
	Obstruction of urinary tract ..	37	24·3	12–43
	Multiple infarcts	24	33·3	14–58
In 2927 necropsies (control)	..	2927	8·6	6–11
C—All types:				
In cases of unilat. renal atrophy	Chr. pyelonephritis + obstruction of urinary tract	71	25·4	15–37
Estimates of all types in 5000 necropsies (control)	All	..	9·38	8–12
All types in 5000 necropsies (control) ..	All cases chr. pyelonephritis ..	372	13·4	9–19
	All cases of urinary obstruction..	300	11	7–16

* Calculated from charts of Clopper and Pearson (1934) at the 95% level of probability.

sion of a renal vessel leads in some instances to hypertension; (2) hypertension in some instances leads to unilateral occlusion of the renal vessels. Our figures do not prove or disprove either of these propositions. They just prove an association and give a quantitative assessment of such an association which may be of interest to clinicians concerned with this problem.

Summary

In 5000 consecutive necropsies there were 106 cases of unilateral renal atrophy. Of the 11 cases in which such atrophy was due to stenosis of the renal artery, " malignant " hypertension was present in 6 and severe essential hypertension in 5.

Of all the cases of " malignant " hypertension in the 5000 necropsies, 1 in 6 was associated with unilateral renal atrophy. Though these figures do not prove that occlusion of the renal artery causes hypertension, they provide quantitative evidence of the association between the two conditions.

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POSTOPERATIVE THROMBOSIS AND PLASMA FIBRINOLYTIC ACTIVITY

A Comparative Study in Africans, Indians, and Whites

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POSTOPERATIVE venous thrombosis and pulmonary embolism are rare in African and Indian patients in this hospital, and the low incidence reflected by the clinical records and necropsy examinations in a six-year period (1953–58) is set out in tables I–III. Coon and Coller (1959), for example, report an overall incidence of 13·8%

TABLE I—INCIDENCE OF PULMONARY EMBOLISM IN INDIAN AND AFRICAN PATIENTS (KING EDWARD VIII HOSPITAL, DURBAN, 1953–58)

Racial group	Sex	No. of cases	Predisposing factor
African* ..	F	4	1 followed radical mastectomy 3 followed gynæcological op.
		2	Postpartum
		2	Medical illnesses
	M	2	Medical illnesses
Total ..		10‡	
Indian† ..	F	1	Pregnancy
	M	1	Following lumbar sympathectomy
		2	Medical illnesses
Total ..		4§	

*Total admissions, 280,000; total operations, 60,000; incidence of postoperative pulmonary embolism, 1 in 15,000.
†Total admissions, 46,700; total operations, 27,000; incidence of postoperative pulmonary embolism, 1 in 27,000.
‡5 (4 postoperative, 1 non-surgical) diagnoses proved at necropsy; 5 clinical diagnoses, with 1 death (deep-vein thrombosis and X-ray). Mortality 60%.
§1 (postoperative) proved at necropsy; 3 clinical diagnoses, with 1 death. Mortality 50%.

TABLE II—INCIDENCE OF DEEP-VEIN THROMBOSIS IN INDIAN AND AFRICAN PATIENTS (KING EDWARD VIII HOSPITAL, DURBAN, 1953–58)

Racial group	Sex	No. of cases	Predisposing factor
African* ..	F	2	1 after gynæcological op., 1 after surgical op.
		6	Antepartum
		11	Postpartum
		21	Medical illnesses
	M	15	Medical illnesses
Total ..		55	
Indian† ..	F	1	Following gynæcological op.
		1	Antepartum
		3	Postpartum
		4	Medical illnesses
	M	3	Medical illnesses
Total ..		12	

*Total operations, 60,000; total cases, 55; incidence of postoperative venous thrombosis, 1 in 30,000.
†Total operations, 27,000; total cases, 12; incidence of postoperative venous thrombosis, 1 in 27,000.

of pulmonary emboli in 4395 necropsies at the University of Michigan and point out that the diagnosis was made clinically in only 12·9% of proven necropsy cases.

Following the observations of Gillman et al. (1957) and Merskey et al. (1958), who have shown higher levels of fibrinolytic activity in Africans than in whites, it was thought that this low incidence of postoperative thromboembolism might be explained by differences in blood-clotting and clot-lysis in the three racial groups—Africans, Indians, and whites. Fibrinolytic activity in these three groups in Durban was therefore studied,

TABLE III—INCIDENCE OF PULMONARY EMBOLISM AT NECROPSY (KING EDWARD VIII HOSPITAL, DURBAN, 1953–58)

Racial group	Sex	No. of cases	Predisposing factor
African* ..	F	3	Following gynæcological op.
		1	Following surgical op.
		20	Medical illnesses
	M	11	Medical illnesses
Total ..		35	
Indian† ..	F	1	Following op.
	M	..	
Total ..		1	

*Total necropsies, 4527. Incidence of pulmonary embolism at necropsy, 1 in 129; incidence of postoperative pulmonary embolism at necropsy, 1 in 1132.
†Total necropsies, 279. Incidence of pulmonary embolism at necropsy, 1 in 279; incidence of postoperative pulmonary embolism at necropsy, 1 in 279.

with special reference to changes in these levels during and after operation.

Materials and Methods

The control group consisted of 23 Africans and 10 Indians (hospital staff and students), and 11 white patients admitted on account of minor complaints.

The group undergoing surgical operations consisted of 36 Africans, 7 Indians, and 11 whites. The operations performed included hernial repair, mastectomy, thyroidectomy, œsophagectomy, and cholecystectomy.

Samples of blood were withdrawn before operation. During each operation samples were taken: (*a*) immediately after the induction of anæsthesia; and (*b*) at hourly intervals thereafter for 4–6 hours. Thereafter specimens were taken daily for 8–10 days. Owing to clinical difficulties, it was not always possible to take samples on all these occasions. In whites, only preoperative and postoperative specimens were taken, none being obtained during operation.

Two samples of peripheral venous blood were obtained on each occasion; for fibrinolytic activity 4 ml. of blood was drawn into a syringe containing 1 ml. of 3·8% sodium citrate and immediately stored on melting ice; for plasma-fibrinogen estimations, 3 ml. blood was collected in an oxalate tube.

TABLE IV—EUGLOBULIN-LYSIS TIMES

Group	Euglobulin-lysis time (min.)			
	No. of cases	Mean	S.D.	S.E.
African staff (students, nurses, porters, &c.)	23	66·7	20·74	4·41
African patients (" cold " cases)	35	104·3	52·04	8·93
African patients (preop.)	16	79·4	45·49	11·75
Indian staff	9	171·1	91·74	32·53
Indian patients (preop.)	7	131·4	78·63	32·09
White patients (" cold " cases)	10	152·0	43·1	14·4

Fibrinolytic activity was determined in duplicate as euglobulin-lysis time (E.L.T.) (von Kaulla and Schultz 1958) all analyses being commenced within 40 minutes of collection. Fibrinogen levels were estimated according to the technique of Folin and Ciocalteau (1927), and were performed on all white patients but not in all African and Indian cases.

Results

The mean E.L.T. for the control groups are shown in table IV. It will be seen that the mean E.L.T. in whites was 152 min.—a level higher than in either an African staff control group eating an approximate white diet (67 min.) or the poorly fed African patient control group (104 min.). By the t-test these differencies were significant at the 2% level. The mean level in Indian staff members (171 min.)

TABLE V—EUGLOBULIN-LYSIS TIME (MINUTES) (MEAN ± S.E.)

Group	No. of cases	Preoperative	During operation	Postoperative	
				1st 48 hr.	3–8 days
African	16	79·4 ± 11·7	75 ± 9·3	134·4 ± 30·5	117·3 ± 17·1
Indian	7	131·4 ± 32·1	101·7 ± 26·1	244·3 ± 61·6	147·1 ± 25·9
White	10	152 ± 14·4	..	189 ± 17·3	127 ± 13·8

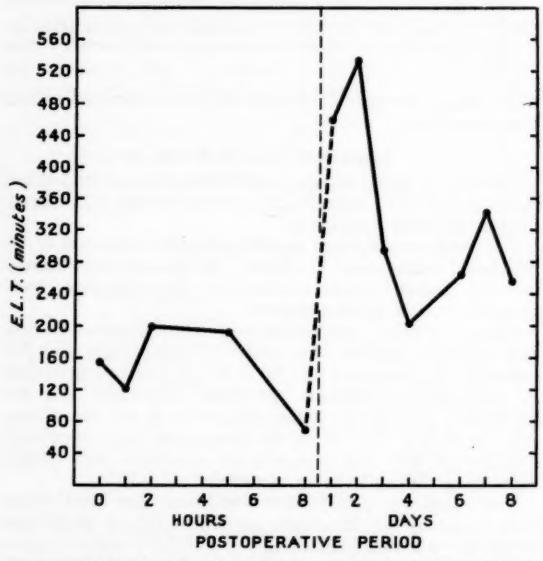
and preoperative cases (131 min.) were not significantly different from the level found in white patients.

Changes in Fibrinolytic Activity Induced by Operations

In 33 patients the E.L.T. was measured before operation, during the first 2 postoperative days, and during the 3rd to 8th postoperative days. In addition, in the African group the E.L.T. was determined during operation. Sex, presence or absence of shock, and length or severity of operation were not found to influence the overall changes in fibrinolytic activity; hence no separate analyses of these factors are included in the results.

There were fairly wide variations in E.L.T. and in the number of determinations performed on some of the patients, and, in order to facilitate analysis, the mean E.L.T. for each of the periods (preoperative, operative, postoperative 0–2 days, postoperative 3–8 days) was determined for each patient. This procedure resulted in some loss of information, but on the other hand made possible a comparison of the broad trends in each group.

From table V it will be seen that in the African patients there was no difference between the mean operative and preoperative levels. In all groups of patients there was an increase in E.L.T. during the first 2 postoperative days compared with the preoperative levels, followed by a fall in E.L.T. during the next 6 days to approximately basal levels (see figure).



Pattern of fibrinolytic activity after operation (mastectomy) in an Indian woman.

TABLE VI—PLASMA-FIBRINOGEN LEVELS (mg. PER 100 ml.) (MEAN ± S.E.)

Group	No. of cases	Preoperative	During operation	Postoperative	
				0–2 days	3–8 days
African	7	202·9 ± 26·6	182·9 ± 29	350 ± 29	338·6 ± 18·7
Indian	2	(1) 200 (2) 420	(1) 150 (2) 360	(1) 320 (2) 360	(1) 350 (2) 370
White	11	215·5 ± 20·4	..	275 ± 40·1	315·8 ± 20·3

In attempting to assess the statistical significance of these results, the mean E.L.T. during the first 2 postoperative days was compared in each of the 33 cases with the respective mean preoperative value; using the Wilcoxan test (Siegel 1956), the differences were found to be significant ($P < 0.01$). The values during the 3rd to 8th postoperative days, however, were not significantly different from those before operation.

The plasma-fibrinogen levels were significantly increased in the African patients in the postoperative period compared to preoperative levels ($P < 0.001$), but no significant change occurred during the operative period (table VI). There were too few estimations on Indian cases to draw any conclusion; the white patients showed an increase in plasma-fibrinogen level during the postoperative period, similar to that found in the African patients.

Discussion

The values obtained for plasma-fibrinolytic activity may be erroneously high if there are associated low fibrinogen levels. Such low levels (resulting from conditions such as chronic liver damage) were excluded in our study by estimating plasma-fibrinogen levels, which in all three racial groups fell within accepted normal levels for whites.

The higher levels of fibrinolytic activity observed in our control series of otherwise healthy Africans, as compared with the white control group, conforms with the findings of Gillman et al. (1957) and Merskey et al. (1958). The reason for increased fibrinolytic activity in the African is as yet unknown. The low incidence of all forms of thrombosis and embolism in Africans, however, may eventually be shown to be at least partly attributable to this high level of fibrinolytic activity.

Increased fibrinolytic activity has been reported following shock and trauma; severe burns; pulmonary, pancreatic, and thyroid surgery, (Cliffton et al. 1956, Cliffton 1958); severe exercise; and the injection of adrenaline. Other workers, using different techniques, have reported

variable results from estimating the effect of diet, liver cirrhosis, trauma, shock, and operation on fibrinolytic activity (Stefanini and Dameshek 1955, Fearnley 1956, Greig 1956, Kwaan et al. 1956, Kwaan and McFadzean 1956, Kwaan 1957).

MacFarlane and Biggs (1946), using a clot-lysis test which distinguished between the presence and the absence of fibrinolysis, found that the proportion of the cases showing fibrinolysis increased during operation, and fell on the immediate postoperative day. The relatively stable levels of fibrinolytic activity found by us in African patients during operation contrasts with these observations. Furthermore, the decrease in fibrinolytic activity, significant in the African group during the first 2 postoperative days, appears to support MacFarlane and Biggs' contention that shock is not a major factor in the activation of fibrinolysin.

Cliffton (1958) has confirmed an occasional increase in fibrinolytic activity following preoperative fear, as reported by MacFarlane and Biggs (1946) and Latner (1947). A similar increase was demonstrated during air raids in the 1939–45 war. The only patient in this series who presented clinically as an extremely anxious individual was an African male who had had a perforated peptic ulcer and recurrent exacerbations associated with periods of work stress, and who was later subjected to vagotomy and antrectomy. In this patient fibrinolytic activity increased greatly before, during, and after operation.

It is well recognised that following trauma there is a significant rise in plasma-fibrinogen level, reaching a maximum several days after. This postoperative increase is confirmed in both African and white patients in this series.

We have shown a decrease in plasma-fibrinolytic activity, and an increase in fibrinogen levels, immediately after operation in all three racial groups. It is difficult to correlate these findings with the rarity of postoperative thromboembolism in Africans and Indians, in contrast to our white patients, who are as susceptible to postoperative thromboembolism as other reported groups. This series includes no cases in which postoperative thromboembolism developed at any time. A detailed study in such cases of all the components of both the clotting and the fibrinolytic mechanisms might throw further light on the pathogenesis of thromboembolism.

Summary

Venous thrombosis and pulmonary embolism occurs so rarely in African and Indian patients in Natal as to be an almost unknown surgical complication.

Control levels of plasma-fibrinolytic activity and fibrinogen were estimated. Fibrinolytic activity was approximately twice as high in a healthy African control group as it was in white or Indian controls. Plasma-fibrinogen levels in the three groups fell within accepted normal levels for white patients.

During operation there was no significant change in fibrinolytic activity in Indian and African patients.

In all three racial groups fibrinolytic activity decreased in the first 48 hours after operation, but tended to rise in the following 6 days.

Postoperatively, fibrinogen levels increased in African and white patients.

Our thanks are due to Prof. J. Wainwright for necropsy records; to Mr. C. J. Lockett and Mr. Moodley for biochemical estimations; and to Dr. S. Disler, medical superintendent, for access to our case-records.

References at foot of next column

SKELETAL FLUOROSIS AND ITS NEUROLOGICAL COMPLICATIONS *

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THE word "fluorosis" was first used by the Danish workers Møller and Gudjonsson (1932) for a form of osteosclerosis caused by industrial exposure to fluorine. Fluorine is one of the trace elements, but under certain circumstances excessive quantities of fluorine may accumulate in the body—particularly in the bones. This chronic fluoride intoxication is usually due to excessive intake of fluoride-rich water. It is also a well-known industrial hazard (Roholm 1937).

Endemic fluorosis due to fluoride-rich water has been recorded in India (Shortt et al. 1937a and b, Pandit et al. 1940a and b, Khan and Wig 1945, Venkateswarlu et al. 1952), in China (Lyth 1946), and in the United States (Smith et al. 1935, Largent and Heyroth 1949). In India, where the pioneer work was done by Shortt and his colleagues, the southern states contain an extensive belt with high-fluoride water and soil (Pandit et al. 1940 a and b, Siddiqui 1955, Satyanarayanamurthi et al. 1953).

The neurological complications of endemic fluorosis have received scant attention, and we first became interested in this aspect while investigating obscure cases of paraplegia, associated with increased density of the spine and other bones, in Punjab—a northern state of India. Almost all the patients came from a small area of Punjab and had in fact skeletal fluorosis with compression paraplegia.

Survey in Bhatinda

We therefore carried out a field survey in the Bhatinda district. This part of the Punjab is very hot in summer, the temperature reaching 115°F (46·1°C). The soil is sandy and the chief sources of water are wells. The general standard of living is poor and the methods of sewage disposal are unhygienic.

Every tenth house was surveyed, and adults over 30 were scrutinised for bony exostoses, stiffness, and limitation of movements in the spine and other joints, and evidence of

* Based on a paper read at the 6th International Congress of Internal Medicine, Basle, on Aug. 24, 1960.

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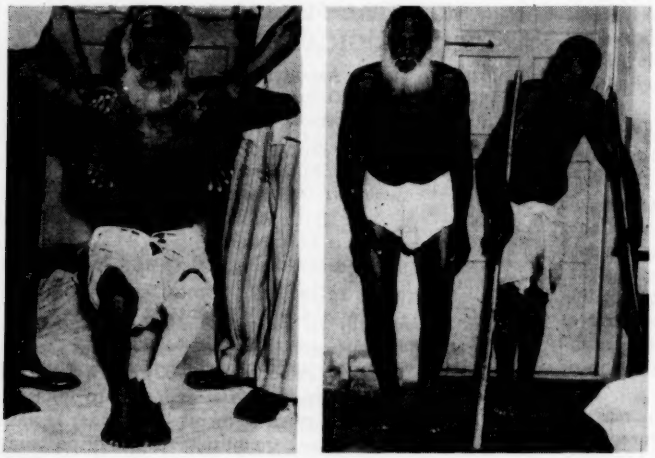

Fig. 1—Skeletal fluorosis with paraplegia. The man on the left has fixed flexion deformity of the knees.

dental fluorosis. Radiographs of all cases with positive clinical features were taken with a standard exposure. Water and soil samples from different parts of this region were analysed for fluoride content. The results varied, but the fluorine content of the drinking-water was uniformly high—as much as 14 parts per million in places. The variations were striking: in one village (Bajakhana) there are two different communities, using independent sources of water. Among the *jat sikhs*, who are comparatively well off economically and have a number of separate wells for their own use, there was no fluorosis. The Harijans—an abjectly poor class working as labourers—used water from a particular well for many years, and many of them have stiff and bent backs. 15 cases of skeletal fluorosis were detected among them.

In this survey, 1696 people were examined out of a total population of 36,000, and 24 cases of fluorosis were detected, and were later confirmed radiologically. 22 other people with skeletal fluorosis sought admission to hospital at various times, so that a total of 46 cases were investigated in detail. Radiographs of almost the whole of the skeleton were taken in every case. The following blood constituents were estimated: urea, sugar, calcium, phosphorus, and alkaline-phosphatase; and the fluoride content of blood, urine, and bone-ash was estimated by titration with thorium nitrate.

In most cases an open bone-biopsy from the tibia was studied histologically and chemically for fluoride content.

Patients with neurological complications also underwent the investigations usual in paraplegia—e.g., cerebrospinal-fluid examination, myelography, and serological tests for syphilis.

Fig. 2—Children from area where 90% of population have mottled teeth.

Findings

Of the 46 patients with skeletal fluorosis, 21 had paraplegia. 43 were men and 3 women. Ages ranged from 35 to 75 (average 51·6). 21 men were farmers and 20 labourers, so that a high proportion of the group were doing manual work.

The onset was always insidious, and stiffness of the back and legs was a universal complaint. Almost all the patients complained of vague fleeting pains all over the body, particularly in the spine and in the knee-joints. In the neurological cases there was increasing weakness of the legs, and 10 patients became completely bed-ridden (fig. 1). Most of the patients had a moderately good diet, perhaps somewhat deficient in animal proteins.

Dental and Skeletal Changes

Fairly advanced dental fluorosis was present in 38 patients who had lived in the endemic area while their permanent teeth were erupting. Fluorosis was of grade-II severity in 18, showing white opacities or patches on the enamel, with faint yellow lines and distinct brown staining, resembling the appearances described by Murray and Wilson (1942), Pillai (1938), Spira (1942), and Shorie (1945).

20 cases showed grade-III dental fluorosis, in which, besides the well-established brown lines, there is considerable pitting all over the enamel (fig. 2). 25% of cases, however, did not show any mottling —an interesting point, because dental fluorosis is generally assumed to be a sensitive indicator of fluoride intoxication. In the field-survey work, as much as 90% of the population had mottled teeth.

As well as these dental changes, there was limitation and slowness of movements of various joints, particularly in the lumbodorsal and cervical regions of the spine and in the hip-joint. There was an almost complete immobility of the thoracic cage, so that the respiratory excursions were reduced. Another helpful clinical sign, which (when present) was diagnostic, was the detection of bony exostoses along the palpable borders of long bones or near the olecranon process. Such bony nodules varied from the size of a sago grain to that of a walnut. They were observed in 6 cases. The skeletal changes, and their associated complications, led to various deformities in 30 cases (kyphosis in 20, flexion deformity of the hip-joints in 4, and flexion deformity of knees in 6).

Fig. 3—Grade-III changes in lumbo-dorsal spine: extreme osteosclerosis, lipping, and osteophytosis, resulting in compression paraplegia.

Radiological Features

There was a generalised osteosclerosis resembling that

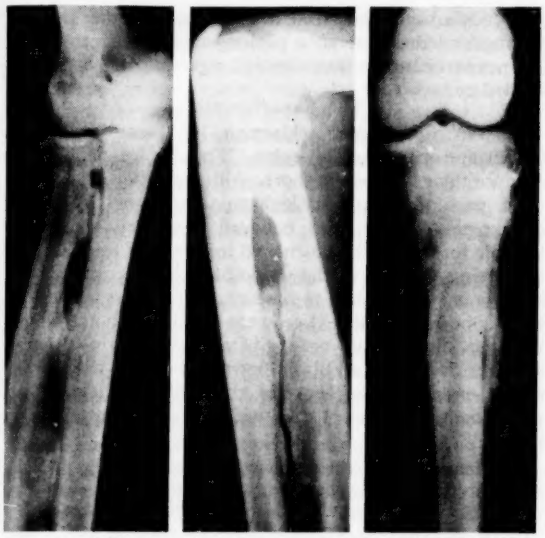

Fig. 4.—Calcification of interosseous membrane and tendon insertions.

described by Roholm (1937), Shortt et al. (1937a and b), and Khan and Wig (1954).

The bony changes were of grade III in 30 cases, grade II in 10, and grade I in 6. In the very early stage (grade I), the cancellous bones showed accentuation of trabecular pattern with a little increase in radiological density. Only the pelvis and spine were affected at this stage. In grade II, the trabeculæ coalesced and appeared granular or amorphous. The bony lesions at this stage were mainly confined to the pelvis, spine, and skull, and the bones of the extremities were still in grade I. Still later, when the disease was much further advanced (grade III), the sclerosis was complete and the bones appeared structureless and chalky.

Such changes were most pronounced in the spine, particularly in the cervical region. There was irregular new bone formation with considerable lipping and osteophytosis (fig. 3). The interspinous and other spinal ligaments were calcified, simulating spondylitis ankylopoietica. This accounted for the difficulty of entering the subarachnoid space for a lumbar puncture. Radiographs of the chest showed a peculiar contrast between a chalky-white bony cage and radiolucent lungs. In the pelvis, there was considerable sclerosis of the iliac crest and ischial tuberosity, and the margins of the sacrum showed exostosis. In advanced cases there was ossification of the sacrospinal and sacrotuberous ligaments. The cortex of the long bones was dense and thick and the marrow-cavity was narrowed by endosteal bone formation. Irregular periosteal bone formation was noticed along the insertions of tendons and ligaments, and also along the attachments of fascia and the interosseous membrane in the forearms and legs (fig. 4).

FLUORIDE CONTENT (g.) OF SAMPLES

Case no.	Soil (mg. per 100 g.)	Water (mg. per 100 ml.)	Blood (mg. per 100 ml.)	Urine (mg. per 100 ml.)	Bone (mg. per 100 g.)
Normal	..	Less than 0·1	Traces	Less than 0·1	Less than 30
Neurological Cases					
1	6·7	1·4	..	0·48	70
2	..	0·35	0·46	..	..
3	..	0·12	..	1·8	..
7	6·7	1·4	..	0·66	..
8	8·5	1·0	0·56	0·35	60
9	..	0·13	..	0·45	..
10	..	..	..	0·67	..
11	..	1·0	0·18	0·56	..
14	..	1·0	0·05	0·175	240
15	..	0·90	0·06	0·233	330
16	..	0·358	0·17	..	..
17	..	0·90	0·06	0·736	..
18	..	0·45	0·20	2·55	100
21	..	0·64	0·06	0·575	680
Non-neurological Cases					
22	..	0·64	0·13	1·04	350
23	..	0·35	..	..	..
24	..	0·22	..	..	..
25	..	0·22	0·11	..	..
26	..	0·138	0·08	0·83	..
27	..	0·182	0·32	0·57	..
28	..	0·167	0·18	0·42	..
29	..	0·188	0·11	0·32	..
30	..	0·27	0·12	0·42	..

The degree of sclerosis was related to duration of intoxication and the level of fluoride in water. Physical strain may also contribute, because the disease was found predominantly in manual workers, who showed involvement of cervical spine and skull—a condition rarely seen by Roholm (1937).

Neurological Features

Compression paraplegia was present in 21 cases. In addition to the symptoms of pure skeletal fluorosis, these patients complained of tingling and numbness of the extremities and other paræsthesiæ, motor weakness, and hesitancy or precipitancy of micturition. There was progressive incapacity owing to weakness, so that 10 patients were almost completely bed-ridden.

The paraplegia was like any compression paraplegia. At first, it was only a paraplegia in extension; but paraplegia in flexion gradually followed. Paræsthesiæ and pain in the limbs were almost universal complaints, although objective sensory disturbances were detected in only 14, and took the form of lost or diminished sensation below a sharply localised level. The deep reflexes were always exaggerated in all limbs, depending on the level of the lesion. The plantar response was extensor in 16, equivocal in 3, and flexor in 2. The abdominal reflexes were lost in 16 cases. There was no evidence of the auditory-nerve dysfunction described by Siddiqui (1955). Hesitancy or precipitancy of micturition was present in 15.

The neurological manifestations are the result of deposition of fluoride in the spine, leading to narrowing of the spinal canal and compression of the cord. There appeared to be no direct toxic effect of fluoride on the nervous system, but this aspect of fluoride intoxication needs further investigation.

Laboratory Data

No significant abnormalities were found in blood, urine, or stools, or in urea-clearance tests. Lumbar or cisternal puncture was possible in only 8 cases, because the ossification of interspinous ligaments usually made it impossible to enter the subarachnoid space. In these 8 cases, the only abnormality was an increase of proteins in 2, resembling a typical Froin's syndrome. There were no changes in chlorides, sugar, or cellular content of the cerebrospinal fluid. Cisternal or spinal myelography was possible in only 2 cases: in one there was considerable delay in the transit of the dye in the cervical region; and in the other there was a complete block at D8.

There were no significant changes in the blood levels of proteins, urea, calcium, phosphorus, or alkaline-phosphotase. The total 24-hour urinary calcium excretion was also normal.

Significantly high levels of fluoride were detected in the drinking-water and soil samples, and in the urine, blood, and bone-ash of the patients, as compared with normal (see table). The bone biopsy showed a characteristic picture of skeletal fluorosis, with disordered lamellæ and an enlarged poorly formed haversion system, resembling the appearances of fluorosis in experimental animals (Weatherell and Weidmann 1959).

Summary

Of 46 cases of skeletal fluorosis in Punjab, India, 21 had compression paraplegia. All the patients lived in a small

area where drinking-water and soil had an extremely high (though variable) content of fluoride.

The intoxication chiefly affected the skeleton, producing typical radiological features of diagnostic value. The teeth also showed characteristic mottling in many cases.

The paraplegia was caused by compression of the spinal cord produced by excessive deposition of fluorides in the vertebral column and resultant narrowing of the spinal canal. It did not differ significantly from other compression paraplegias.

Significantly high levels of fluoride were found in the blood, urine, and bones of these patients; and there was a characteristic histological pattern of skeletal fluorosis.

We are indebted to Dr. J. B. Sirivastva and to Dr. P. Devi, of the Central Research Institute, Kasauli, for the fluoride estimations. Our thanks are also due to Dr. S. Singh for the help with case-records and the field survey, and to Shri G. S. Sekhon for the photographs.

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MUTATION, CANCER, AND AGEING

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IRRADIATION of living things by ionising radiation can result in mutation, cancer, and ageing (Hempelmann and Hoffman 1953, Upton 1957). Probably the most important means by which radiation is believed to produce its biological effects is through dissociation of water with the formation of the chemically active free radicals, HO· and HO_2·. (Stein and Weiss 1948). These same free radicals might be expected to be produced during the course of the major energy-gaining reactions employed by living things—the reduction of molecular oxygen to water and the conversion of light energy to chemical energy. Also, since reactions involving free radicals are in general not " clean-cut ", some of these free radicals might be expected to produce side-effects through more or less random reaction with cellular components. The presence of free radicals in living systems has been shown by electron paramagnetic-resonance absorption studies (Commoner et al. 1954 and 1957, Ingram 1958). Further, the concentration of free radicals has been shown to increase with increasing metabolic activity in conformity with the hypothesis that free radicals are involved in biological oxidation-reduction reactions (Michaelis 1951, Waters 1946).

If ageing does involve attack on the organism by free radicals as suggested, an increase in the concentration in the organism of compounds, such as mercaptans, capable of reacting rapidly with free radicals, might decrease the rate of attack on constituents such as desoxyribosenucleic acid (D.N.A.) and thus lead to a decrease in the rate of ageing, and therefore to a prolongation of effective life. Two experiments to investigate this possibility have been carried out.

The Experiments

The first experiment (Harman 1957) employed AKR (male) and C3H (female) mice. These mice were used because their life span is short. Although they die for the most part of lymphatic leukæmia (AKR) or mammary carcinoma (C3H), it was believed that they would be suitable for testing the postulated influence of free radicals on ageing; since, if the hypothesis was correct, the average age at which the neoplastic process appeared should be increased. Mice were obtained shortly after weaning, divided into groups of about 30 (10 per cage), and then fed daily (ad lib.) a powdered diet to which was added either nothing or else the hydrochloride of an antioxidant. The mice were weighed and counted every month.

AKR mice receiving cysteine hydrochloride (1·0% w), 2-mercaptoethylamine hydrochloride (1·0% w), or 2, 2′-diaminodiethyl disulphide dihydrochloride (0·5% w) had a half-survival time (age by which 50% of the animals were dead) of 10·5, 10·5, and 10·6 months respectively, whereas that of the controls was 7·6 months—a prolongation of about 35% ($P < 0.01$). The influence of these compounds is not on the leukæmia which the AKRs develop, as shown by the fact that all but one of the blood-smears taken at 12 and 13 months were normal. The mouse from which the abnormal smear was taken was moribund. Further, the weight gains of the control and treated mice were essentially the same. Ascorbic acid (2% w) and 2-mercaptoethanol (0·5% w) were also studied; neither prolonged life. None of the five compounds tested had any definite effect in the C3H mice.

The second experiment (Harman 1960b) utilised Swiss mice (males) in addition to the AKR (males) and C3H (female) strains. Pelleted food—to which either nothing or the hydrochloride of one of four antioxidants was added before pelleting—was used instead of powdered food in hope of maintaining high tissue levels of the additives for longer periods. Fresh batches of food were made up at intervals of 1 to 3 months.

Cysteine hydrochloride (1% w) and hydroxylamine hydrochloride (2% w) increased the half-survival time of the AKR mice from the control figure of 9·6 months to 11·0 and 11·2 months respectively—a prolongation of about 15%. 2-Mercaptoethylamine hydrochloride (1% w) did not increase the life span—for some reason the members of this group of AKR mice had a relatively high mortality in the early months of the experiment. 2, 2′-diaminodiethyl disulphide was apparently toxic at the level employed (1% w) for this as well as the other two strains of mice.

2-Mercaptoethylamine hydrochloride (1% w) increased the half-survival time of C3H mice from a control value of 14·5 months to 18·3 months—an increase of 26% ($P < 0.01$). There was some indication (decreased mortality-rate) during the early months of the first experiment that 2-mercaptoethylamine might lengthen the life span; the pronounced effect in the second experiment may be in part due to the difference in the mode of feeding. Hydroxylamine hydrochloride (1% w) slightly prolonged the half-survival time from 14·5 months to 15·5 months—an increase of about 7%. In this, as in the first experiment, cysteine hydrochloride (1% w) did not prolong life.

None of the antioxidants studied lengthened the life span of the Swiss mice.

Discussion

These two experiments are encouraging and justify further exploratory studies of antioxidants as anti-ageing agents; several additional antioxidants, shown to protect mice against multiple sublethal doses of X-radiation

(Ershoff and Stern 1960), are now under study in the AKR, C3H, and Swiss mice. In addition, the magnitude of the life-prolonging effect, particularly that of 2-mercaptoethylamine hydrochloride, suggests that endogenously produced free radicals play a major part in ageing.

These results agree with those of a human study (Chope and Preslow 1956) which indicates that older persons with low blood-levels of vitamin A and ascorbic acid (both easily oxidised compounds) have a higher mortality-rate than do persons with greater amounts of these substances in the blood.

The concept that free radicals are involved in ageing was applied to the fact that the rate of ageing as measured by the logarithm of the mortality-rate increases with advancing age. Part of this effect could be due to a decrease in the level of antioxidants—for example, mercaptans—in the body with increasing age. A study of the serum-mercaptan concentration as a function of age agreed with this possibility (Harman 1960a). The serum concentration of mercaptan groups of normal men decreased with age from a level of about 55 μmoles per 100 ml. of serum at age 20–40 to about 40 μmoles per 100 ml. at 80. The data for women are of the same magnitude and show the same trend. The serum concentration of another antioxidant, ascorbic acid, likewise has been reported to decrease with age in men (Kirk 1954).

Thus, on both theoretical and experimental grounds, there is firm support for the hypothesis that endogenously produced free radicals play a prominent part in mutation, cancer, and ageing.

Summary

Mutation, cancer, and ageing are attributed basically to the side-effects of endogenously formed free radicals.

Experimental work on ageing based on this hypothesis has been encouraging. Several antioxidants were found to increase the half-survival time of AKR and C3H mice; the prolongation with 2-mercaptoethylamine was about 20%. Serum-mercaptan levels, as predicted by the free-radical hypothesis, were found to decrease with age.

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Preliminary Communication

LUCANTHONE RESINATES IN SCHISTOSOMIASIS

LUCANTHONE hydrochloride (' Miracil D ') was introduced [1] for oral treatment of schistosomiasis. It is 1-β-diethylaminoethylamino-4-methylthioxanthone hydrochloride. It has been successfully used for twelve years, in which its main drawback has always been the severity of gastrointestinal side-effects. There have been several attempts to present lucanthone in a less irritant form,[2 3] but the hydrochloride remains in general use.

The description by Abrahams and Linnell [4] of oral depot therapy with drug resinates suggested that lucanthone resinates might produce adequate blood-levels without the unpleasant side-effects associated with the hydrochloride. Prof. W. H. Linnell kindly arranged for two different lucanthone resinates to be supplied for laboratory trials. The lucanthone was combined with ' Zeocarb 225 H ' resin of 1% and 8% cross-linkage. The plasma levels after single doses equivalent to 1 g. of lucanthone base were estimated by an acetone-ether extraction method [5] in baboons and in man. Satisfactory blood-levels were obtained with the 1% cross-linkage compound but not with the 8% compound, and side-effects were minimal.

When the same resinates were given, in doses of 1 g. lucanthone equivalent twice daily for three days, to patients in East Africa, the 1% cross-linkage resinate maintained a curative blood-level of over 0·5 mg. per 100 ml.[6] but the 8% resinate did not. Cures were obtained with the 1% resinate, and side-effects were not troublesome. When further supplies of lucanthone resinates were available, trials were begun on East African patients in Kenya.

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METHODS

Two compounds were used—a 1% cross-linkage resin containing 36·4% lucanthone, and a 2% cross-linkage resin containing 41·3% lucanthone. The dose of the 1% resinate was dispensed in three cachets and provided the equivalent of 1 g. of lucanthone. The 2% resinate was given in doses of three cachets containing a total of 0·9 g. of lucanthone. All doses were given under personal supervision.

COMPARISON OF SIDE-EFFECTS DURING ONE COURSE OF TREATMENT WITH HYDROCHLORIDE AND RESINATE OF LUCANTHONE IN AFRICAN ADULTS

Side-effects	6 g. hydrochloride: no. affected among 11 patients	12·1 g. resinate 2% cross-linkage*: no. affected among 24 patients
Nil	1†	16
Vomiting	7	2
Nausea	10	3
Anorexia	8	2
Epigastric discomfort or pain	6	6
Vertigo	6	0
Depression	2	0
Prostrate	3	0
Toxic psychosis	1	0

*=5·4 g. of base. † Incomplete course.

Adult patients infected with *Schistosoma hæmatobium* and *S. mansoni* were chosen for their high output of viable eggs and their normal renal function. After treatment, urine or fæces were examined on each of three consecutive days monthly for two or three months by microscopy, a hatching technique, and rectal biopsy.[7] Plasma levels were estimated, in most cases, at intervals of one or two days.

RESULTS

Lucanthone Resinate 1% Cross-linkage

Eight patients were treated by the lucanthone equivalent of 1 g. twice daily for three days, and the results were compared with those in eight patients treated with lucanthone hydrochloride on the same dosage schedule.

Plasma levels from patients receiving resinate were in general satisfactory, but showed greater individual varia-

7. Davis, A. *E. Afr. med. J.* (in the press).

tion than the levels in patients treated with the hydrochloride. Side-effects were greatly reduced in the resinate series, but the impression was gained that the drug was released too quickly from the resin. In addition, there were fewer complete cures among the resinate patients.

Lucanthone Resinate 2% Cross-linkage

The plasma levels after single doses, equivalent to 3 g., 2 g., and 1 g. of lucanthone, were studied daily. Only the 3 g. dose produced a plasma level of over 0·5 mg. per 100 ml.; and a dosage scheme of 3 g. on the first day, 2 g. on the second day, and 1 g. on the third day was adopted. This maintained a steady plasma level of 0·5–0·7 mg. per 100 ml. for at least five days.

Twenty-four African men with pronounced *S. mansoni* infection were given one course of treatment. Thirteen patients were free of eggs after a month, but at three months only seven were still free. This result is similar to that produced by a single course of treatment with 6 g. of the hydrochloride.[3] The risk of preinfection and reinfection was always present.

The resinate greatly reduced the frequency of side-effects; but the reduction in their severity, not shown in the accompanying table, was equally satisfactory. In fact, three of the patients recorded as having symptoms complained only of slight nausea and epigastric discomfort lasting a few hours, and they could almost have been placed in the " no side-effects " group.

CONCLUSION

These results suggest that one course of treatment with the 2% resinate may prove acceptable and effective for most hæmatobium infections and that two courses may be needed for mansoni infections. A full account of investigations of these resinates will be published elsewhere, but clearly the reduction of side-effects will make it possible for patients who are intolerant of the hydrochloride to receive adequate lucanthone treatment.

The lucanthone resinates were supplied by the courtesy of Aspro-Nicholas Ltd., Slough.

Bilharzia Research Group,
Medical Research Council

A. DAVIS
M.B. Durh., M.R.C.P.E.

New Inventions

A SEMI-AUTOMATIC STITCHING DEVICE

THE operation of aortoiliac thromboendarterectomy requires careful close suturing of the arterial incision; usually a continuous over-and-over stitch at 1 mm. intervals is inserted with a fine atraumatic needle mounted with arterial silk. The incision is often 20 cm. long and the insertion of some 200 stitches needs intense and protracted concentration by the surgeon. The new instrument (fig. 1) is designed to release the needle from its holder, pick up the far end to draw it through, and reset the needle in the holder in readiness for the next stitch.

The instrument has two pairs of small needle-holding jaws. In the resting position the thread-end of the needle is held by one pair of jaws and the second pair is retracted; when the operating lever (A in fig. 1) is compressed, the second pair of jaws come down to grip the needle near its point and the first pair release their grip and retreat; relaxation of the operating lever reverses the action. Thus the instrument can be made to change its grip from one end of the needle to the other without at any time losing its hold. Only rough usage causing bending of the needle can interfere with this action. Because the needle in this semi-automatic needleholder is not at any time " free ", there is no need to employ the opposite hand to hold or steady the needle whilst " transferring " the needleholder; the needle can be passed with one hand and the only skilled movement is that of introducing the needle into the tissue at the exact point required.

In practice, the needle is inserted through the tissue (figs. 2a and b) and the operating lever is pressed so that the needle is now gripped on the portion already protruding through the tissue (figs. 2c and d); the needle is then drawn through completely (fig. 2e), and the operating lever relaxed so that all is set for drawing through the thread and for the next stitch. A locking device (B in fig. 1) is fitted which allows movement of only the forward pair of jaws when the operating lever is pressed; in this way the needle can be removed or inserted into the instrument. The needleholder can be adjusted before use to grip either a straight 25 mm. arterial needle or a 25 mm. curved arterial needle specially designed for the instrument. The curved needle is flattened on its inner and outer surfaces to prevent rotation.

This instrument has been used in about 30 operations upon human subjects, not only to close longitudinal incisions in arteries but also to perform end-to-end anastomosis during replacement of aortic aneurysms by a prosthesis. The needleholder has proved most reliable; dropping the needle was an unusual event and most operations were completed without " losing " the needle once.

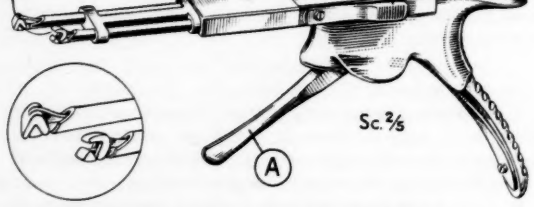

Fig. 1—The semi-automatic needleholder.
A. The operating lever. B. The " needle-release button " which locks the second pair of jaws in a retracted position.

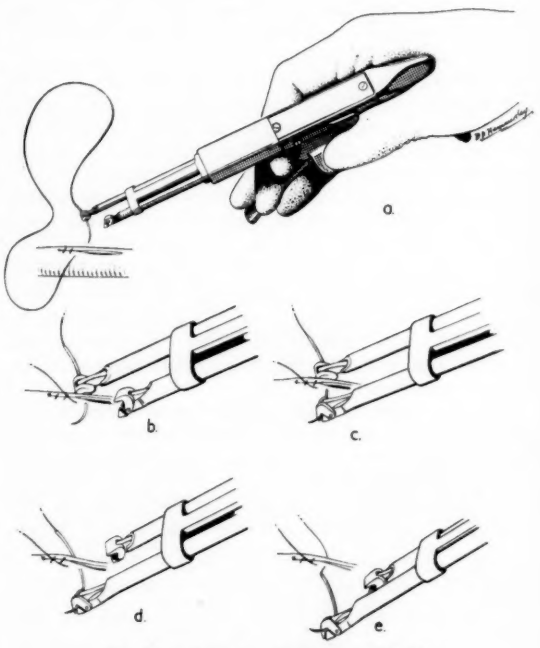

Fig. 2a-e—Steps in using the needleholder.

We particularly recommend this instrument for thromboendarterectomy. No doubt there are other fields where the surgeon using a fine needle at a depth would appreciate it. At present its use is limited to either a straight needle or, more usually, the special curved needle; but an alternative version, capable of handling a bigger and stronger curved needle is to be designed.

Very little practice is needed to learn how to use this instrument, provided care is taken to avoid straining the needle. With practice many additional manœuvres are learnt which greatly enhance its usefulness. For example, if the tissue is unusually tough, the needle can be inserted initially with the second pair of jaws down gripping it near the point at its most highly tempered portion and reducing any tendency to bend it by angulation; relaxation of the operating lever, further insertion of the needle and pressure on the operating lever enable the needle to be drawn through completely. Although primarily designed for a " forehand " action, the needle can be reversed for a " backhand " action. The instrument can be used either in the right or left hand, but in the latter case the needle-release button which is operated by the thumb cannot easily be used without transferring the instrument to the right hand. The makers are prepared to modify it for the left-handed surgeon.

We are indebted to D. P. Hammersley and H. S. Brain for the illustrations.

The final design and manufacture of this instrument in stainless steel has been sponsored by the National Research Development Corporation. It is manufactured by Messrs. C. F. Thackray, Park Street, Leeds, who also supply the special curved arterial atraumatic needle and silk in sterile ampoules. We should like to thank Mr. A. B. Hallam of Messrs. Thackray for his most skilful interpretation in stainless steel of our original design and for suggesting many valuable modifications in detail.

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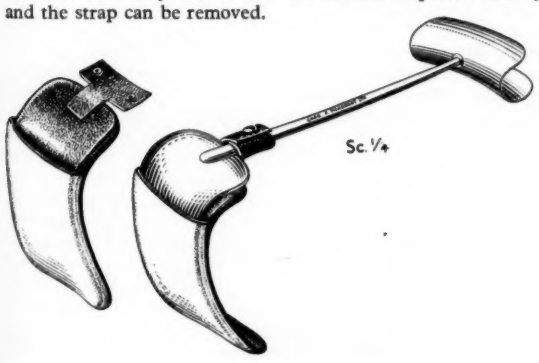
A LIVER-RETRACTOR PAD

IN difficult cholecystectomies and other operations on the biliary tract, the liver is not uncommonly damaged by prolonged or excessive retraction. This can be obviated to some extent if a folded abdominal swab is applied to the liver surface under the retractor, but this sometimes becomes displaced and obtrudes into the operation field.

To prevent damage to the liver a rubber pad has been devised in the form of a sock, which fits over a Kelly or Dyball retractor (the types most commonly used) and which can be sterilised by boiling. It has sponge rubber padding $^1/_4$ in. thick on its underside, and white rubber on its outer surface, which, by reflection, aids the illumination of the wound. In addition (as will be seen from the figure) the sock is fitted with a small rubber strap and press-stud to fasten it to the handle of the retractor, although experience may show that the sock fits the retractor so closely that it does not become displaced in use, and the strap can be removed.



A similar pad could, of course, be designed for any other retractor where firm pressure might cause injury to underlying tissues.

I am much indebted to Chas. F. Thackray, Ltd., of 10, Park Street, Leeds, 1, for their assistance in the design, and for making experiments with suitable materials for this appliance.

The Infirmary,
Rochdale

A. M. MCMASTER
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Reviews of Books

Valvular Disease of the Heart in Old Age

P. D. BEDFORD, M.D., M.R.C.P., consultant physician, F. I. CAIRD, D.M., M.R.C.P., medical registrar, Cowley Road Hospital, Oxford. London: J. & A. Churchill. 1960. Pp. 194. 30*s*.

THIS admirable book is a study of 419 patients with valvular heart-disease admitted to the Oxford Geriatric Unit over a period of six years. There are chapters on rheumatic heart-disease (mitral incompetence being commoner than mitral stenosis in old age), aortic stenosis, syphilitic aortic incompetence, and " isolated aortic incompetence " (what was formerly called arteriosclerotic or functional aortic incompetence), a subject which has never been singled out for special study in the past and which here forms one of the most original and valuable contributions in this book. The authors did their own postmortems, and this gives special value to their clinical and pathological findings. In later chapters the complications, treatment, and prognosis of the various lesions are discussed. Throughout, the relevant literature is carefully and critically considered, and there are nearly 400 references. The book ends with a useful appendix on statistical methods and the construction of life-tables for follow-up studies.

This model of a well-constructed monograph will be the envy of many who have written a thesis: it is concise, comprehensive, accurate, critical, and well illustrated, and will do much to raise the prestige of geriatric medicine in this country. It is exceptional value for money.

An Outline of Chemical Genetics

BERNARD S. STRAUSS, PH.D., associate professor of microbiology, University of Chicago, Chicago, Illinois. Philadelphia and London: W. B. Saunders. 1960. Pp. 188. 35*s*.

THE pages of this and other journals testify to the increased interest in conditions caused by hereditary rather than environmental influences. Unfortunately, except for some awareness of mendelian inheritance, many doctors are unfamiliar with the principles of genetics. While a visiting professor at Osaka University, Dr. Strauss was invited to give a series of lectures on chemical genetics to graduate students in the faculty of medicine. This book is the outcome of these lectures, and it can be praised almost unreservedly.

An opening chapter on the genetic control of protein synthesis is followed by one on the chemical nature of the hereditary material, in which there is an excellent introduction to D.N.A., its chemical structure, and its distribution during chromosomal duplication. These key problems in biology are discussed informatively with frequent reference to modern work. Information obtained from neurospora and other lower organisms is often neglected by those interested primarily in human biology, and the author's discussion on qualitative changes in enzyme structure as a result of gene action in neurospora is therefore particularly valuable. Some 24 allelic mutants of the tryptophane synthetase locus in *Escherichia coli* have been recognised and illustrate the complexity of the control of a single biochemical reaction. The chapter on mutation is well balanced and includes a discussion on the possible ways in which mutagens act. The number of chemicals to which man is exposed, and which have been shown to cause mutations in fungi, bacteria, or drosophila, is considerable. Whether these substances are mutagenic in man is not known but experiments in mammals are needed. The chapter on biochemical genetics in man is concise without loss of accuracy.

Many of the classical inborn errors of metabolism are discussed intelligently from the viewpoint of intermediary metabolism. Fig. 19 is a topographical representation of the variation in concentration of substances in urine and of the taste sensitivity to different substances in several individuals: it is a remnant of the past which could have been omitted.

The virtues of this monograph are many and the defects few. The subject matter is well chosen and composed in an easy and flowing style. It is pleasant to recommend an introductory book, informative and relatively inexpensive, which conveys some of the excitement of recent discoveries in genetics.

Dentistry for the Pre-School Child

G. N. DAVIES, D.D.S., associate professor and head of the department of preventive, public health, and children's dentistry, University of Otago Dental School, New Zealand; RICHARD M. KING, B.D.S., M.S., lecturer in children's dentistry, University of Otago Dental School, New Zealand. Edinburgh: E. & S. Livingstone. 1961. Pp. 268. 32*s*. 6*d*.

WHILE there is no shortage of excellent textbooks—both English and American—on children's dentistry, there are few that deal with the dental care of the very young child. The authors of this book are particularly well qualified to fill this gap, since most of their patients are pre-school children. Dental surgeons—apart from the dedicated few in the school dental service—tend to fight shy of the very young patient, and this book is meant to stimulate a greater interest in dental problems at this age. As the authors point out, the dental profession must not only recognise the dental needs of the pre-school child, but must also be prepared to do something about them.

The advice on the management of the child in the surgery could be read with advantage by all, because much of it can usefully be applied to far older children. As Davies and King imply, a child attends for some form of dental treatment and not for "nice rides in the chair". Experience suggests that this approach rarely achieves much except to waste the time of all concerned.

Diet and nutrition are dealt with in some detail, and this chapter should provide the answers to most of the questions asked by parents about the effect of diet on the dentition. A particularly valuable chapter discusses the diseases of children which have oral manifestations or which may affect the treatment to be given; and this section is a helpful reminder that the teeth and buccal cavity form only a small part of the whole body.

The emphasis is deliberately and rightly on principles rather than methods. Mere technical skill is not enough—the basic principles underlying the child's dental problems must be understood.

Interceptive orthodontics and the causes and prevention of dental caries are treated at length. The advice on the treatment of grossly carious deciduous teeth is sensible, and the authors recognise that there is a limit beyond which conservation is useless or unwise.

The illustrations are well-chosen and clear, and the extensive references at the end of each chapter are up to date. A minor criticism is that some proprietary drugs and preparations are given the names by which they are known in New Zealand, and so may cause momentary perplexity to English readers.

The Nucleic Acids

Vol. III. Editors: ERWIN CHARGAFF, department of biochemistry, Columbia University, New York; J. N. DAVIDSON, department of biochemistry, University of Glasgow. New York and London: Academic Press. 1960. Pp. 588. 128*s*. 6*d*.

IT is five years since the first two volumes of the "nucleic acids" were published and the two editors were faced with the problem of keeping their material up to date. They have done so by producing this third volume which is by a new group of authors and deals with advances since 1955 and matters which were not fully covered at that time. The first six chapters are chemical rather than biological and concern deoxynucleic acids as macromolecules, the synthesis in vitro of polynucleotides and nucleic acids of microorganisms and viruses. The last six chapters are more biological and deal with the biosynthesis of nucleic acids and proteins, agents which influence nucleic-acid metabolism and the effect of radiations. Two of the contributors are from Moscow, two each from Great Britain and France, five from the U.S.A., and one each from Germany, Poland, and Canada—an international party.

Those who are familiar with volumes I and II will certainly need volume III. The metabolism of nucleic acid has become a highly specialised study, but the editors are to be congratulated on the comparative simplicity of this book. Most of it is within the compass of the advanced student and parts of it are relatively easy reading. The references which are given at the foot of each paper are adequate, but not overwhelming.

Education and Retirement

BRIAN GROOMBRIDGE. London: National Institute of Adult Education. 1960. Pp. 159. 8*s*. 6*d*.

THIS book is well described by its subtitle as "an enquiry into the relevance of leisure in later life". The traditional picture of retirement as an evening of desirable ease after a lifetime of hard work seldom fits the facts. Too often the retired person finds himself facing a whole range of adjustments to a totally new way of life on a much reduced income; and the idea that a man or woman needs education to cope with these problems is a comparatively new one, more familiar in America than in this country.

Mr. Groombridge's report investigates the extent to which existing facilities for adult education, including clubs, and all forms of technical, scientific, and artistic societies are being used to help people to enrich their retirement. It is not surprising to learn that those who take advantage of such things are mainly those who are already better educated than the average, and ways still need to be developed to interest others less fortunate.

No very clear picture emerges of how this is to be done, but the author has performed a useful service in reminding us of the many activities available to the elderly to help in these difficulties, which will certainly loom larger in the future.

Controlled Clinical Trials (Oxford: Blackwell Scientific Publications. 1960. Pp. 177. 20*s*.).—This book contains the papers delivered at a conference held in Vienna in March, 1959, under the auspices of the Council for International Organisations of Medical Sciences. The organiser and chairman was Prof. A. Bradford Hill. The purpose of the conference was to summarise the British approach to controlled trials, and all the speakers came from this country. The collected papers provide a useful description of the aims, difficulties, and achievements of controlled trials in medicine.

Babies by Choice or by Chance (London: Victor Gollancz. 1960. Pp. 191. 12*s*. 6*d*.).—This book, whose first author, Dr. Alan F. Guttmacher, is an American gynæcologist, is much more than the handbook of contraception its title may suggest. It describes all the existing means of encouraging, preventing, preserving, or terminating pregnancy, with full technical detail but, mercifully, not the usual diagrams, and discusses their indications and implications, merits and defects from the viewpoint of an experienced, humane, thoughtful, and sometimes indignant medical man. It has been admirably anglicised by its second author, Dr. Eleanor Mears, medical secretary of the Family Planning Association, who occasionally indicates difference of practice or opinion by brackets; but it is essentially an American book. This is strikingly apparent in the widespread acceptance of A.I.D., warmly approved of and discriminatingly practised by Dr. Guttmacher, and by the special confusion arising from each state of the Union having its own abortion law. Dr. Guttmacher pleads for general and detailed sexual education, to include conception control; research for a contraceptive to stem the force of the population explosion; reform of abortion law (he favours decision by special boards); and in general the application of clear heads and kind hearts to the fertility problems that confront us as human beings and world citizens. He gives ample reason for at least this last plea and, in many respects, the matter is urgent.

THE LANCET

LONDON 28 JANUARY 1961

Autoimmunity and Immunotransfusion in Burns

LAST year, discussing toxæmia in burns,[1] in the light of new work we raised the old question whether absorption of non-bacterial toxins from the burned skin is a possible cause of illness and death. FEODEROV and his colleagues [2–4] in Moscow had claimed that the body was flooded with antigens (which they believed to be toxic) derived from the burned skin, having detected these in the blood of recently burned patients and experimentally burned animals for up to about fourteen days after burning; thereafter antibodies to the antigens appeared in the blood. The serological methods used included prolonged complement fixation in the cold, which, unless special care is taken, may give non-specific reactions; and we suggested that confirmation by other, more sensitive, methods was necessary.

Confirmation of aspects of this work has come from two sources. First PAVKOVA et al.,[5 6] of the burns unit in Prague, found by the sensitive technique of collodion-particle agglutination that, when an extract of unburned skin from burned patients was used as an antigen, antibodies were detectable in the blood between the fourth and eighth days after burning. The titre reached a peak about the fifteenth day, then gradually declined as the patient's condition improved and antibody reappeared in convalescence. Secondly, ROSENTHAL et al.[7 8] in Chicago report that sera from recently burned patients contain toxic substances which they call "cytotoxin" and "cytolysin" according to the effects tested. Cytotoxin was detected by the ability of the sera to inhibit the growth of Hela cell suspensions after seventy-two to ninety-six hours in tissue-culture, and cytolysin by the lytic effect on the patient's red blood-cells either of serum from the patient in the presence of guineapig serum (complement) or of serum from those with healed burns. "Antitoxins" to these were demonstrated in the sera of those who had recovered from burns, mainly by ability of the sera to neutralise the cytotoxic effect of sera from patients with recent burns. Interesting and important though this work is, some of the techniques are not above criticism—including the detection of lysin (antigen) and hæmolysin (antibody) apparently by the same method, and the use as a substrate of blood from patients with burns. The red blood-cells of patients with recent burns has increased fragility to saline and may undergo partial spontaneous lysis.[9]

Notwithstanding criticisms of technique, it seems reasonable to conclude that serological changes do occur in patients with burns; but not all these changes are necessarily immunologically specific: at least some are possibly related to, or associated with, the rise of γ-globulins often found after burning, no doubt owing to bacterial infection. Possibly too, some of the response is "non-specific" in the same sense that false-positive Wassermann reactions may be found in various non-syphilitic conditions—though the same serological explanation is not necessarily valid. The work needs to be pursued with some of the newer sensitive serological techniques, including perhaps the anti-globulin methods of COOMBS.

The aspect of the reports from Moscow, Prague, and Chicago which will most interest clinicians is that concerned with the therapeutic transfusion of plasma or blood from patients with healed or healing burns. This therapy has developed out of the idea that passive transfer of the skin-antibodies would neutralise the "toxic" antigens flooding into blood from the burned skin. PUSHKAR [10] reports that donor blood was collected from those with healed burns (the donors had burns covering more than 7% of the body area) and was given either as plasma or whole blood as soon as possible after the accident, and always within forty-eight hours. 100–400 ml. was given every day in the first week after burning. Clinically impressive results are claimed, including the disappearance of "toxæmic" symptoms. Some of this benefit may be due to the transfusion of plasma or blood per se or to the combating of bacterial infection through the passive transfer of antibacterial antibodies arising after infection of the burn in the donors. ROSENTHAL [7] carried out a pilot trial with this "immunotherapy" in 6 burned children. The donor blood was collected from patients who had recovered from extensive burns (25% or more of the body area) months or years previously, and was given from the fourteenth day onwards after burning. (The delay was apparently not deliberate and seems to have been due to the time needed to obtain the special blood.) Repeated transfusions of 250 ml. of plasma or 500 ml. of blood were given. These workers, too, claim beneficial results, including reduction of pyrexia and general clinical improvement. Some of the effects were dramatic, but were shortlived unless further transfusion was given. In Prague, too, transfusion of blood or plasma from those with healed burns has been tried in a few cases, and the Czechoslovak workers are impressed with the clinical effects.

Encouraging though these reports are, further experience is needed before the value of this treatment can be regarded as established. The history of burns therapy is marked by many forms of treatment—such as tannic acid, adrenocortical extract, cortisone, and corticotrophin—which at first were acclaimed but in the end

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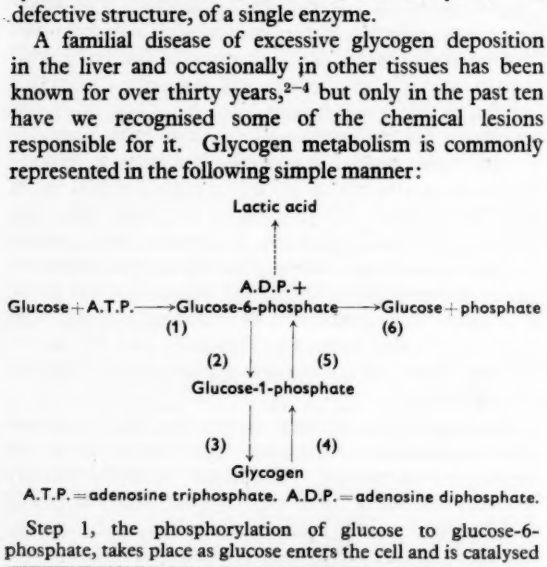
proved disappointing. A controlled clinical trial is called for. This should be carried out on carefully selected cases—preferably in children in the first place, because of their smaller blood-volume and therapeutic needs. They would be divided into concurrent " test " and " control " series in an unbiased way. The difficulty is likely to be that of obtaining enough of the special adult donors. A widespread campaign through the various regional blood-transfusion centres may be needed in order to obtain enough, and then the plasma might be centralised at one or another of our burns units for the trial. If this therapy is proved to be beneficial, a special group of blood-donors may have to be organised, comprising those with healed burns and possibly some actively immunised with extracts of skin.

Diseases of Glycogen Storage

THE body humours lasted a thousand years: nowadays those intellectual fancies which we dignify as " new concepts of disease " come and go with the regularity of academic quinquennia. It is almost a shock to realise that GARROD's concept of inborn errors of metabolism [1] has already outlived the half-century. To the original quartet of errors—albinism, alkaptonuria, cystinuria, and pentosuria—we could add today over fifty conditions which would satisfy GARROD's criteria; and most such diseases can be assigned to one of three groups. The hæmoglobinopathies are so far the only ones in which the lesions have been tracked down to abnormal amino-acid sequences of single protein molecules, perhaps the direct imprints of inherited mutant genes. At the other extreme we can but dimly perceive the inborn chemical errors in such common metabolic diseases as diabetes or gout. In between is that exciting group of illnesses in which step by step we can now trace the clinical syndrome to the defective action, but not yet to the defective structure, of a single enzyme.

A familial disease of excessive glycogen deposition in the liver and occasionally in other tissues has been known for over thirty years,[2–4] but only in the past ten have we recognised some of the chemical lesions responsible for it. Glycogen metabolism is commonly represented in the following simple manner:



A.T.P. = adenosine triphosphate. A.D.P. = adenosine diphosphate.

Step 1, the phosphorylation of glucose to glucose-6-phosphate, takes place as glucose enters the cell and is catalysed by the enzyme, hexokinase. Steps 2 and 5 are catalysed by the same enzyme, phosphoglucomutase; but steps 3 and 4 require the collaboration of two enzymes each. In step 3 a phosphorylase removes the phosphate groups from the glucose-1-phosphate molecules and attaches the bared first carbon atoms to the tail end of a glycogen nidus. When a chain has reached the critical length of eight glucose residues, a second enzyme establishes a branch-point by converting an α-1-4 to an α-1-6 linkage. This " brancher " enzyme determines the characteristic tree-like structure of the glycogen molecule. In step 4 a phosphorylase splits off the phosphate groups from the outermost tier of glucose units, and a " debrancher " enzyme catalyses the cleavage of the α-1-6 linkages at the branch-points. Step 6 represents the final release of glucose from the cell, and many metabolic paths converge on it: it is catalysed by the enzyme, glucose-6-phosphatase.

Among the enzymes involved in glycogen metabolism, the phosphorylases differ from one tissue to another, and even in a single organ they probably exist in both active and inactive forms; and their activation depends on distant hormonal influences as well as on local changes.[5–7] Of glycogen itself it has been said that no two molecules are identical in any one individual: their disparity in weight, size, and branching pattern is clearly reflected in the varied amounts which can be extracted from the same tissue by different techniques; and stable and unstable fractions may have distinct physiological roles.[8–10] It is hardly surprising, therefore, that our metabolic scheme should have several weaknesses and at least one major flaw. One of its weaknesses is that it accounts for changes in the quantity of body glycogen only by molecular growth and shrinkage: the way in which new seeds of glycogen arise, either from existing molecules or from oligosaccharides, remains unknown. Its major flaw is that it represents glycogen synthesis as the mirror image of glycogen breakdown; and for some years now this test-tube assumption has been contradicted both by animal experiments and by clinical findings. Adrenaline and glucagon—hormones which enhance phosphorylase activity [11]—both favour glycogen breakdown; and there is no reason why the activation of an enzyme which catalyses a reversible reaction should always have a unidirectional effect.[12] Similarly, high concentrations of K^+ in rat-liver slices favour glycogenesis, while high concentrations of Na^+ activate phosphorylase and promote glycogenolysis.[13] Such observations have led to the discovery of a pathway for glycogen synthesis which depends for the provision of α-1-4-glucosidic units, not on glucose-1-phosphate (and phosphorylase), but on a complex hexose nucleotide, uridine diphosphate glucose (U.D.P.G.).[14–18] This substance can be broken down

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to uridine diphosphate (U.D.P.) by the enzyme U.D.P.G.-transferase; and the reaction is closely linked to the important energy-yielding mechanism of uridine-diphosphate/uridine-triphosphate interconversion.

Much is heard nowadays of biochemical advances serving clinical medicine; but the reverse is no less true. The most convincing evidence yet for an independent pathway of glycogen synthesis in living organisms has come from clinical and metabolic studies of patients with glycogen-storage disease. These investigations began in the 1920s when SCHÖNHEIMER found that in glycogenosis the glycogen deposit remained stable in vitro unless it was treated with normal liver tissue [19]; and this eventually led CORI and CORI to identify by direct assay the cause as an inborn deficiency of the key enzyme, glucose-6-phosphatase.[20] The defect interferes with the normal generation of blood-glucose from liver-glycogen, and it accounts for the patient's negative response to injected adrenaline and glucagon. (Injection of adrenaline is still the most dependable diagnostic test when liver tissue is not available for analysis.) In common with most metabolic errors, the block also leads to a high serum concentration of intermediate metabolites; and WAGNER et al. have made the interesting suggestion that the low reducing power of intermediate hexose-phosphates, compared to that of free glucose, partly explains the habitually low blood-sugar levels in most cases.[21 22] (These phosphates, unlike glucose, cannot penetrate the cell membrane; and the cells "starve amid plenty".) More recently HSIA and GAWRANSKA have reported abnormally high fructose-phosphate levels in symptomless carriers of the gene.[23]

Besides this comparatively common metabolic error (type 1), at least five other chemical lesions have been found to cause glycogenosis.[7 24] Type 2 is a rapidly lethal condition in which glycogen is deposited in most tissues, especially heart and skeletal muscle: its enzyme mechanism is obscure, but family studies suggest transmission by a recessive gene.[25–27] In type 3 the deposited liver-glycogen, on treatment with purified phosphorylase, yields characteristic outer-chain lengths of 4–5, instead of the normal 8–9, glucose residues; and the cause has been identified as a deficiency of the "debrancher" enzyme.[28–30] (An ætiological link between these seemingly distinct "types" is suggested by the findings in an affected sibling of a type-3 case: careful chemical analysis of preserved liver tissue showed that the deposited glycogen had a normal structure but that glucose-6-phosphatase activity was greatly diminished.[31]) Since phosphorylase is not lacking in type-3 glycogenosis, glycogen is broken down to a polysaccharide which closely resembles phosphorylase-limit dextrin: hence the alternative and more precise name, "limit-dextrinosis". Our knowledge of type 4 rests mainly on ANDERSEN's report of a 17-month-old infant who died of cirrhosis of the liver. End-group analysis of the deposited polysaccharide showed greatly increased outer-chain lengths and a diminished number of branching-points, suggesting a deficiency of the "brancher" enzyme.[32] A muscular form of the disease may also exist.[33] Type 5 is a somewhat nebulous entity, characterised by deposition of structurally normal glycogen in skeletal but not in cardiac muscle.[7 27] Type 6 is of particular biochemical interest, for it seems to result from tissue-specific phosphorylase deficiency; and glycogen deposition in the presence of such a defect strongly supports the idea that the phosphorylases are predominantly catabolic enzymes.[7] In HERS' cases hepatic glycogenosis was associated with normal brancher-enzyme and glucose-6-phosphatase but much-reduced liver-phosphorylase activity [30]; while MOMMAERTS et al.[34] and SCHMID et al.[35] described cases of "progressive myopathy" in which the skeletal muscles were loaded with glycogen and virtually devoid of phosphorylase.

In the glycogeneses Nature confronts us with difficult clinical problems and often with tragic case-histories; but they also represent fascinating metabolic experiments. The regulation of enzyme activity in the body—the links between hormones, enzymes, and homœostasis—are among the biochemist's most immediate concerns today; and the intelligent interpretation of fluctuations in the clinical course may provide the clue which the laboratory worker and ultimately the clinician need.

Salt and Water Retention in Heart-failure

ONE feature of right-sided heart-failure is retention of salt and water and the development of œdema. Many factors have been thought to account for this disturbance, but no single one has so far been found to be invariably present. Sodium retention has been ascribed to a fall in glomerular filtration-rate; but, although acute changes in glomerular filtration profoundly affect sodium balance,[36] chronic lowering of the filtration-rate is not associated with sodium retention,[37] and this rate is not lowered in all patients with heart-failure and œdema.[38 39] Both in the healthy and in patients with cardiac failure more than 99% of the filtered sodium is reabsorbed. If the proportion of filtered sodium which is reabsorbed remains unchanged, a fall in filtration-rate of 1 ml. per minute will lead to the retention of 2 mEq. of sodium per day. It is possible, therefore, for a fall in glomerular filtration to lead eventually to sodium retention; but the normal response to an increase in sodium in the body is altered control of tubular reabsorption, and where this does not occur in

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patients with cardiac failure this homœostatic mechanism must be defective. On the other hand some patients with heart-failure retain much more sodium than can be accounted for by the change in filtration-rate. It seems probable, therefore, that patients with cardiac failure and œdema have excessive tubular reabsorption of sodium.

Sodium is reabsorbed at four different points along the tubule. Firstly, in the proximal convoluted tubule about 80–85% of the filtered fluid is reabsorbed. Probably the sodium is transported actively, and the water may well be carried passively.[40] The active transport of sodium in the ascending limb of the loop of Henle is an essential part of the countercurrent mechanism for the concentration of urine.[41] In the distal convoluted tubule sodium and potassium ions are exchanged, leading to reabsorption of sodium in proportion to the potassium lost.[42] Finally sodium is reabsorbed in the collecting ducts where it is exchanged for ammonium ions.[43]

The exchange of sodium for potassium in the distal tubule is controlled by aldosterone from the adrenal cortex. This hormone is the most effective naturally secreted sodium-retaining hormone. In an extensive review of salt and water retention in heart-failure DAVIS [44] concludes that aldosterone is pre-eminently important in the formation of œdema in heart-failure. The relation of aldosterone secretion to alteration in hæmodynamic functions is now well established. Although the final factor acting on the adrenal cortex to cause increased secretion of aldosterone is a humoral agent [45] other than corticotrophin, it is becoming apparent that corticotrophin has an important synergistic role.[46] The afferent nervous pathways mediating changes in blood volume and pressure and changes in aldosterone secretion are complex. They have been carefully worked out in the dog; and in man, although the details may be different, the principles are probably the same. An increase in aldosterone secretion is brought about by a small fall in the pulse-pressure [47] at the junction of the thyroid and carotid arteries [48]; but an increase in arterial pulse-pressure will not lower aldosterone secretion. The mechanism by which aldosterone secretion is lowered involves quite different nervous pathways. The receptors probably lie in the region of the right auricle [49 50] and send their impulses up the vagal nerves.[51] This vagal mechanism—the "turn-off mechanism"—cannot operate to increase aldosterone if the thyrocarotid junction is denervated.[52] Indeed constriction of the carotid arteries then causes a fall in aldosterone because the reflex hypertension produced is associated with a rise in right atrial pulse-pressure.[52]

Whenever the heart is failing the arterial pulse-pressure will tend to fall; this will be compensated by increased autonomic tone. The fall in pulse-pressure will also stimulate aldosterone secretion. In most cases of left ventricular failure the aldosterone excretion is not high,[53] presumably because the "turn-off" mechanism operates normally. In right-sided heart-failure there will be the same stimulus to aldosterone secretion, but apparently in this case the "turn-off" mechanism does not operate normally because aldosterone secretion is sometimes increased.[53 54]

Continued administration of aldosterone or other sodium-retaining steroids to healthy people does not lead to continued sodium retention; nor is continued retention found in patients with aldosterone-secreting tumours. Sodium retention is shortlived and is replaced by potassium excretion. The nature of this switch-over from sodium retention to potassium excretion, which has been referred to as the "escape mechanism",[55] is still undecided. In the first few days of administration of aldosterone some sodium retention occurs, and the hormone is presumably then acting at a site in the tubule which is proximal to the sodium-potassium exchange site. Later, when the "escape" has occurred, sufficient sodium must reach this exchange site to allow the excretion of excessive amounts of potassium.

If aldosterone is given to patients with œdema, progressive sodium retention occurs,[56] and there is no switch-over to potassium loss. Presumably sodium is reabsorbed proximally so that little reaches the exchange site. This denotes that in patients with œdema sodium retention is caused by a primary defect other than in aldosterone secretion. The production of aldosterone in excess would then make the condition worse. Nevertheless SHARPEY-SCHAFER and MILLS [57] have found that some patients with hypertension who go into heart-failure and some patients with mitral incompetence who are in severe heart-failure excrete water and salt loads normally.

The means by which sodium is reabsorbed by the proximal tubule is unknown. Such reabsorption cannot be regulated only by aldosterone because there must be alteration in proximal tubular reabsorption to operate the "escape mechanism". Another humoral agent influencing sodium reabsorption by the tubule has been described by MILLS et al.[58] Possibly this acts on the proximal tubule where a very small percentage change in reabsorption could bring about a very large change in sodium excretion.

That aldosterone is not the most important factor causing sodium retention in heart-failure is also suggested by studies with aldosterone antagonists,

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which block aldosterone at the tubular level; these have remarkably little diuretic action in heart-failure.[59 60]

The excessive proximal reabsorption of fluid in patients with heart-failure has also been investigated by BELL et al.[61] In studies with mannitol they showed that fluid can be transferred by osmotic action from the proximal to the distal tubule, and that aldosterone may then cause potassium excretion when sufficient sodium reaches the exchange site. The hyponatræmia of heart-failure may also be due to excessive proximal reabsorption. The plasma is diluted on ingestion of water. With excessive proximal tubular reabsorption, dilute fluid will be reabsorbed and insufficient volume reaches the distal tubule for " free " water formation.

Studies in patients with essential hypertension have thrown light on another aspect of sodium control. Intravenous administration of saline[62] or of hypertensin[63] causes prompt sodium diuresis in such patients, but not in individuals with normal blood-pressure. This feature can, however, be reproduced in the healthy if they first receive fludrocortisone and saline.[64] In hypertensive patients, as in the normotensive, infusion of hypertensin increases the rate of aldosterone secretion.[65] In normotensive people the increased aldosterone secretion leads to sodium retention, but in the hypertensive the sodium-diuretic action of the hypertensin may exceed the sodium-retaining action of the increased aldosterone secreted.[65]

The evidence suggests that the salt and water retention associated with heart-failure is not primarily a function of altered filtration-rate, nor is it the result mainly of high aldosterone secretion. It is probably due to excessive proximal tubular reabsorption of sodium, but how this mechanism is disturbed in heart-failure is unknown.

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Annotations

RECURRENT FOCAL NEPHRITIS

No classification of glomerulonephritis is universally accepted, since the suggested groups overlap considerably; but the clinical features of acute glomerulonephritis are well recognised, and renal biopsy early in the disease has shown diffuse glomerular changes of varied severity.[1–5] In most patients the presenting features of hæmaturia, proteinuria, œdema, and hypertension appear some two to three weeks after a focal infection—most often streptococcal tonsillitis or otitis media.

Acute glomerulonephritis is commonest between the ages of 5 and 15 years, and the prognosis is best in this group. Ellis[6] reported complete recovery in 80% of 225 patients, 60% of whom were less than 20 years old. 5% died during the acute illness; of the remaining 15%, some died in uræmia within twelve months, and in the rest the disease progressed more slowly to a fatal chronic phase of renal failure. Rudebeck,[7] reviewing the prognosis of acute glomerulonephritis in 356 patients over the age of 10 years, found complete recovery in only 53% and an immediate-mortality rate of 6%. His figures showed that the prognosis was much less favourable over the age of 30 years, in respect both of immediate mortality and of risk of progression to chronic nephritis.

Episodes of hæmaturia, uncomplicated by œdema or hypertension, at the height of acute systemic infections were first described by Scheidemandel[8] and Volhard and Fahr.[9] This apparently benign condition was called " focal nephritis ", since it was believed to represent direct bacterial injury to only a few glomeruli. But there was no histological proof of a focal lesion. Baehr[10] reported recurrence of such attacks in 14 young adults who had sustained or intermittent hæmaturia without œdema, hypertension, or renal failure. He described the condition as " a benign and curable form of acute hæmorrhagic nephritis ", but again the presumptive diagnosis of focal nephritis was unproven histologically. Payne and Illingworth[11] concluded that there was no significant clinical or prognostic difference between " diffuse " and " focal " glomerulonephritis, classified clinically by the presence or absence of œdema, no histological criteria for differentiation being available.

Ross[12] has again suggested that there may be a persistent but benign form of glomerulonephritis, characterised clinically by recurrent episodes of hæmaturia without œdema, hypertension, or renal failure. In all but 1 of the 9 patients studied (their ages at onset ranged from 6 to 25 years) proteinuria became persistent within nine years; but, in follow-up periods ranging from two to thirty-one years, no instance of nitrogen retention was detected. In 1 patient, aged 17, persistent hypertension developed in the ninth year of his disease. Where there was evidence of a preceding bacterial infection, either in the initial or in subsequent episodes, the interval between this infection and the onset of hæmaturia was always less than eight days—a further deviation from the accepted clinical pattern of acute glomerulonephritis. Ross suggests that differentiation on the basis of the patchy nature of the histological lesions in the kidney may be possible. Renal biopsies were performed in 5 of the 9 cases at various stages from the ninth month to the seventh year of the disease. In 3 of these he found inflammatory changes which were " local " within the affected glomeruli, and " focal " within the tissue sampled —a somewhat confusing terminology. In the 4th patient similar cellular changes were more " diffuse " within the glomeruli and " generalised " throughout the kidney—findings presumably indistinguishable from those of acute diffuse glomerulonephritis. The biopsy from the 5th patient showed no significant abnormality.

1. Iversen, P., Bjørneboe, M., Krarup, N. B. *Advanc. intern. Med.* 1954, **6**, 161.
2. Kark, R. M., Muehrcke, R. C., Pirani, C. L., Pollak, V. E. *Ann. intern. Med.* 1955, **43**, 807.
3. Parrish, A. E., Howe, J. S. *Arch. intern. Med.* 1955, **96**, 712.
4. Brun, C., Gormsen, H., Hilden, T., Iversen, P., Raaschou, F. *Acta med. scand.* 1958, **160**, 155.
5. Hutt, M. S. R., Pinniger, J. L., de Wardener, H. E. *Quart. J. Med.* 1958, **27**, 265.
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8. Scheidemandel, E. *Münch. med. Wschr.* 1913, **60**, 1778.
9. Volhard, F., Fahr, T. Die Brightsche Nierenkrankheit. Berlin, 1914.
10. Baehr, G. *J. Amer. med. Ass.* 1926, **86**, 1001.
11. Payne, W. W., Illingworth, R. S. *Quart. J. Med.* 1940, **9**, 37.
12. Ross, J. H. *ibid.* 1960, **29**, 391.

Heptinstall and Joekes [13] found "focal" and "local" histological changes in 13 of 100 consecutive renal biopsies, but their patients did not represent a benign or homogeneous clinical group since the presumptive diagnoses included systemic lupus erythematosus, polyarteritis nodosa, and Henoch-Schönlein purpura.

Ross's histological evidence for a focal glomerular lesion in his patients is as yet less clear-cut than are the clinical grounds for differentiating the condition from typical acute glomerulonephritis. Long follow-up and further renal biopsies in these and similar cases are essential before finally accepting the existence of a truly benign persistent form of glomerulonephritis, associated with histological evidence of focal glomerulitis. Clear definition of a distinct condition with characteristic renal biopsy findings would be important for prognosis in patients with recurrent hæmaturia.

ELECTROLYTE LOSSES DUE TO UREA WITH OPERATIVE TRAUMA

INTRAVENOUS urea is increasingly used by neurosurgeons because of its capacity for shrinking the brain during and sometimes after operations. Its instability is counteracted by mixing it fresh from the dry state; cooling is prevented by simple application of warmth, and hæmolysis by administering it in dextrose solution. How it acts is not clear; but indirect evidence suggests that it does not enter freely into the cells of the brain, the contents of which are therefore hypotonic to the interstitial fluid and blood: they lose water and shrink. Intraocular pressure is also lowered (and accordingly urea is administered for the relief of acute glaucoma). The whole body thereafter loses water by diuresis, which lasts for a few hours. The action is not followed by any "rebound" of cerebral œdema, and a healthy kidney is not damaged. The effect helps to reduce the trauma in retracting the brain for access to deep structures [14–16] or when intracranial pressure is raised by the bulk of a tumour without gross hydrocephalus.

It is important to know what happens to the main electrolytes during and after administration. Glucose and mannitol augment the renal excretion of sodium and chloride as well as of water,[17] but Seldin and Tarail [18] found that comparable amounts of urea produced only minor changes in sodium excretion. These studies were conducted in the absence of operative trauma, which will itself cause retention of sodium.[19] Murphy et al. [20] studied 30 patients subjected to comparable degrees of operative trauma.[21] All received 3 litres of fluid in the subsequent twenty-four hours, but 15 received in 1 of the litres 4% urea and 5% dextrose. On the second and third day all received 3 litres of 5% dextrose solution with 75 mEq. of sodium and chloride. In the first twenty-four-hour period the mean excretion of sodium was nearly four times greater in those patients receiving urea, with a loss of 113 mEq. compared with 28·9 m.Eq. in the control group. Chlorides were also excreted to a significantly greater degree, and potassium to a slightly greater degree, in the treated than in the control group.

13. Heptinstall, R. H., Joekes, A. M. *ibid.* 1959, **28**, 329.
14. Javid, M. *Surg. Clin. N. Amer.* 1958, **38**, 907.
15. Stubbs, J., Pennybacker, J. *Lancet*, 1960, i, 1094.
16. Avman, N., Fisher, R. G. *Surgery*, 1960, **48**, 491.
17. Strauss, M. B. Body Water in Man. Boston, 1957.
18. Seldin, D. W., Tarail, R. *Amer. J. Physiol.* 1949, **156**, 160.
19. Jorgensen, H. E., Schlegel, J. V. *Surg. Gynec. Obstet.* 1959, **108**, 339.
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21. Moore, F. D., Ball, M. R. The Metabolic Response to Surgery. Springfield, Ill., 1952.

In the period of sodium retention after operation the normal diurnal swing of pH is reduced, the urine remaining in a narrow acid range. The urea-treated patients showed a greater diurnal swing than the control group, and this was correlated with the excretion of base induced by the urea. Although water was excreted constantly to a greater extent after urea, there was only rough correspondence between excretion of base ions and volume of urine. This denotes that, although water can be replaced according to urinary output, the degree of saluresis cannot be inferred from the urinary volume or from the amount of urea given. Either the amount of each ion must be analysed directly, or a rough guide obtained by serial estimations of pH. The total amount of sodium excreted in twenty-four hours can be as great as 200 mEq. —the equivalent of about 4 pints of physiological saline solution.

These findings probably need not affect the use of urea in acute glaucoma, but they are relevant to neurosurgical operations—and particularly hypophysectomy, when diabetes insipidus may follow the chemical diuresis. Administration of cortisone or 'Pituitrin' complicates the position. A useful working rule is to give in each eight-hour period a volume equal to the volume of urine excreted in the previous eight hours plus 200 ml., the operative blood-loss having been made up at the time. Some of this fluid should be in the form of saline or Hartmann's solution, and serum electrolytes will give a rough guide to immediate needs if diuresis is prolonged.

HEART-RATE MEASUREMENT IN THE ACTIVE SUBJECT

HEART-RATE recorders are no longer the experimental, often "home-made", instruments of a few years ago.[1] Various types are now available commercially, either alone or in combination with cathode-ray electrocardiographs, cardiac pacemakers, and defibrillators. As was forecast by Grieve,[2] attention is now being given to the problem of cardiotachometry in the active healthy subject. In 1957 the Ministry of Supply developed a heart-beat transmitter with a gated amplifier, which could be worn by soldiers during assault courses.[3] No integrating circuit was provided, and the instrument transmitted a single pulse for each heart-beat.

Hoare and Ivison [4] have now described a new transmitter for measuring the heart-rate of athletes. Their cardiotachometer is designed to operate continuously for at least an hour while transmitting a signal with a range of 300 yards. To eliminate action-potentials from the muscles the instrument has two completely transistorised channels fed from three electrodes, of which one—common to both channels—is attached to the chest. The others are attached to the ear lobes. The signal from the heart-muscle is amplified to about 2 V before being applied to a coincidence circuit which gives an output only when a signal reaches both inputs simultaneously. This gating circuit triggers a monostable multivibrator, the refractory period of which can be adjusted to give additional discrimination against unwanted signals. An audio-frequency subcarrier oscillator, controlled by the multivibrator, modulates the transmitter. No attempt is made to transmit any waveform resembling an electrocardiogram. For field work the received signal is fed to

1. *Lancet*, 1958, i, 956.
2. Grieve, D. W. *New Scientist*, May 7, 1959, p. 1022.
3. Grieve, D. W., Humphries, W. J. A. Ministry of Supply, Directorate of Physiological and Biological Research. Report no. 87. July, 1957.
4. Hoare, D. W., Ivison, J. M. *Electron. Engng*, 1961, **33**, 6.

a transistor ratemeter.[5] The whole instrument, including batteries, weighs 12 oz. and has a 15 in. aerial—a compromise between electrical efficiency and practical limitations of size.

The cardiotachometer has proved satisfactory in recording the heart-rate of middle-distance runners. Tests with sprinters showed some errors, probaby caused by muscle-action potentials. In future designs, this will be overcome by using a three-channel system. More transmitting channels can be added so that respiratory-rate and limb acceleration can be telemetered.

GASTRODIALYSIS

THE administration of too much water or sodium salts is probably commoner than most who administer continuous intravenous infusions are prepared to admit. Removal of such excesses is not easy; when renal function is poor, removal may be very slow, and the ancient method of purging is not always applicable to the elderly patient or after a major abdominal operation. The use of dialysis by running fluid through the peritoneal cavity is limited both in scope and in the occasions on which it is suitable. Dialysis by perfusion of the patient's blood through a semipermeable membrane in a bath of suitable fluid is more widely applicable, but requires expensive apparatus and much skill.

Searching for some effective method short of perfusion, Schloerb and Carr [6] remembered the large daily turnover of secretions in the gastrointestinal tract, the rapid absorption of water from the stomach, and the high rate at which gastric juice equilibrates with blood.[7] Following work on dialysis in the small intestine they have now devised a semipermeable membrane in the form of a collodion-glycerin balloon which can be introduced on a polyvinyl tube through the nose and œsophagus into the stomach. Through the tube 300 ml. of various solutions was instilled into the balloon, where the solution remained for varying periods before being sucked off. Hypertonic dextrose or sucrose solution were used to remove water and urea, and various combinations of glucose and sodium-chloride solution to remove potassium and urea. In healthy subjects, using 300 ml. of solution which was changed every 15 minutes, they were able to remove about 2 mEq. potassium and 25–40 mg. non-protein nitrogen per hour. The rate of removal of potassium is directly related to the concentration gradient between the balloon fluid and the gastric contents, but depends also on the frequency with which the balloon fluid is changed. Gastrodialysis in 3 patients with chronic uræmia did not change the clinical courses significantly. Schloerb and Carr have shown that the amounts of water, sodium, chloride, potassium, non-protein nitrogen, and glucose which were transferred were proportional to the compositions of the dialysates. They suggest that, if dialysis can be maintained for 20 hours each day, 10–44 mEq. potassium, 24–116 mEq. sodium, 280–480 mg. of non-protein nitrogen, and up to 2·5 litres of water can be removed daily. The pattern of extraction can be determined by changes in the composition of the dialysate. The absorption of glucose from the dialysate varied from 130 to 440 g. per day; and by using 50% solution up to 1800 calories could perhaps be supplied each day. They suggest that up to 200 mEq. hydrogen ion can be removed each day—equivalent with the chloride removed to 2 litres of 0·1*N* hydrochloric acid. Potassium is probably removed quickly enough to prevent a rapid rise in the extracellular concentration of potassium but not to reverse established potassium intoxication.

Marr et al.[8] have reported the application of the same principle, using a sheet 'Cellophane' bag instead of a collodion-glycerin balloon. Marr et al. treated 14 patients in acute renal failure by constant perfusion and aspiration. Acidosis was controlled in all their patients, and azotæmia was stabilised in half.

This method has not yet had enough clinical testing to justify its wider adoption, but clearly it demands further study. If by modifying the membrane, the composition of the dialysate, or the manner of circulating the fluid, the rate of exchange (especially of potassium) can be increased, gastrodialysis may clearly offer an attractive alternative to more drastic methods of modifying the composition of the body-fluids.

COITUS AS A CAUSE OF CERVICAL CANCER

A STUDY of factors thought likely to be concerned in the genesis of carcinoma of the cervix uteri, undertaken at the Charity Hospital, New Orleans, has once more drawn attention to the role of coitus in causation.[9] A series of 122 patients known to have squamous carcinoma of the cervix were matched for race (63 Negroes in each group) and five-year age-group with patients with other gynæcological disorders from the same wards. Somewhat surprisingly, of the patients with cancer of the cervix, 5 were aged 25–29 and 9 were aged 30–34. These 14 accounted for as much as 11% of the total of 122, but 4 and 6 respectively were Negroes, which may have a bearing on this relatively high proportion with early onset. (Harnett [10] found only 3% of cases in the 25–34-year age-group in London.) All the patients were interviewed by the same nurse interviewer, who had no knowledge of the patient's condition and who conducted the interview as if it concerned only diagnosis and treatment. The interview included questions on residence, age, pregnancies, use of contraceptives, marital history, sexual relationships, douching practices, and education and occupation of the patient, her husband, and her father.

This study confirms that carcinoma of the cervix is associated with early marriage and with multiple marriages.[11 12] It also suggests an association with extramarital relations, first coitus at an early age, and frequent coitus at all ages. These findings are consistent with the greater incidence of the disease in married than in single women, and with the high incidences in certain population groups—Negroes, Southern white, and those with low incomes—in which early marriage is common.[13] The findings are compatible with the low incidence in nuns and the high incidence in prostitutes.[14]

Terris and Oalmann,[9] speculating on the mechanism of coitus in the genesis of carcinoma of the cervix, suggest that the most likely factor is frequent contact of the cervix with a hypothetical carcinogenic agent over a period of many years; and on rather slender experimental evidence [15] they are inclined to incriminate a component

5. Kitchin, L. D. *ibid.* 1959, **31**, 44.
6. Schloerb, P. R., Carr, M. H. *Surg. Gynec. Obstet.* 1960, **111**, 531.
7. Cope, O., Blatt, H., Ball, M. R. *J. clin. Invest.* 1943, **22**, 111.
8. Marr, T. A., Burnell, J. M., Scribner, B. H. *ibid.* 1960, **39**, 653.
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13. Haenszel, W., Hillhouse, M. *J. nat. Cancer Inst.* 1959, **22**, 1157.
14. Towne, J. E. *Amer. J. Obstet. Gynec.* 1955, **69**, 606.
15. Pratt-Thomas, H. R., Heins, H. C., Latham, E., Dennis, E. J., McIver, F. A. *Cancer*, 1956, **9**, 671.

of smegma. They admit that the data at present available provide no valid information as to the proportion of the patients' husbands who had undergone circumcision, and affirm that only examination of the husbands would accurately establish this. No association was found between carcinoma of the cervix and the number of pregnancies, but childless women were included with the group which had had one or two children. Nor was there any association with the duration and frequency of douching (including douching with coal-tar derivatives) or the use of contraceptives.

It is no easy task to collect a series of over 100 patients with carcinoma of the cervix and to interview them with the care exercised in this study. None the less, more extensive data are needed before these results can be accepted unequivocally.

COMMUNITY STUDIES

THERE have been many recent studies of sociological developments in town and countryside, some based on information collected under the auspices of such organisations as the Institute of Community Studies and the Centre for Urban Studies, which lately issued its first report, *Newcomers*,[1] dealing with the West Indians in London. In 1957 Young and Willmott [2] described their study of *Family and Kinship in East London*, in which they pointed out that the people living in " Greenleigh ", a new council estate on the outskirts of London, tended to be cut off from relatives, suspicious of their neighbours, lonely; the atmosphere there was very different from the warmth and friendliness of Bethnal Green, from which many of them had come. Now the same authors, searching for a London suburb with a high proportion of " middle-class " people, have studied Woodford, and they present their findings in *Family and Class in a London Suburb*.[3] They were anxious to see whether such an area would have a distinctive kind of approach to family and community life: would the people be more isolated, more anxious about status, less sociable with their neighbours? They considered many possible criteria of social class—family connections, education, occupation, income, property, &c., often, though not necessarily, inter-related—but in the main occupation was the criterion used. In concentrating upon occupation, Young and Willmott were following in the footsteps of the Registrar-General and of such earlier investigators as Sir John Sinclair,[4] who, in his account of Scotland at the end of the 19th century, divided the population into three broad groups—the eleven productive classes (including the monied interest class, the class for the fine arts, and the literary class), the eleven useful, or indirectly productive, classes (including politicians, lawyers, doctors, innkeepers, menial servants, and persons who furnished innocent amusements), and the five unproductive classes (the insane, debtors confined, vagrants, criminals, and the like).

In Woodford, 38% of the adults are manual workers and their wives, 62% non-manual; and 76% of those in employment work outside the borough, mostly in London. 68% live in privately owned houses, the density of population being 16 persons per acre, compared with 64 in Bethnal Green. Only some 12% of the present residents were born in the borough: a few came in from the surrounding countryside, but far more came out from the city. For them the move outwards was also a move upwards: " more people flock in from East London because the suburb is desirable and by so doing make it less desirable for those who were there before ". Not surprisingly, the new influx has not always been welcomed. The most respected citizens of the old Woodford moved northwards after the receding countryside or southwards to a watering-place, and even the coming of Sir Winston could not wholly make up for the loss of the old aristocracy.

Sociability in Bethnal Green needs no organisation; there people are vigorously at home in the streets, their public face much the same as their private, but in Woodford they seem to be quieter and more reserved in public. On the other hand, there is in Woodford a far greater development of clubs and social organisations of all sorts which, however, attract " middle-class " much more than " working-class " people, just as the working-class frequent the clubs less than the others and are notably less assiduous in Church attendance. It may well be, as the authors suggest, that many " middle-class " people of the sort who live in Woodford have a certain capacity or skill at " making friends ". Bethnal Greeners do not need this capacity; their friends are ready made. Probably friendliness has not the same character in the two districts. In Bethnal Green people take each other very much for granted, whereas in Woodford relations are not so easy-going; a newcomer to a street will not necessarily be accepted into a neighbourhood group. While it is true that in the main the residents of Woodford feel that they belong to a friendly, helpful community—almost as unanimously, though not as demonstrably, as in Bethnal Green and much more so than at Greenleigh, the municipal housing-estate—there is within their friendships undoubted evidence of social stratification; as the wife of a commercial traveller put it, " Unless you are in the swing, like being an active Conservative, suburbia is *hell*." One interesting finding is that the attitudes of the working-class in Woodford turned out to be different in many ways from those in Bethnal Green, which was a classless or rather a one-class society: in Woodford, confronting a predominantly " middle-class ", the " working-class " tend to divide, some " changing rather unconvincingly to a version of the Bethnal Green code ", some accepting middle-class views and setting out to become middle-class themselves, in outlook, in home and furniture, and in politics. It is true that nowadays objective differences between the classes in Woodford are slighter than they have been in the past. People in different classes spend their money on the same kind of things—on cars, on refrigerators, on washing-machines. The two classes live in the same kind of district, often in the same kind of house, and have much the same kind of hopes for their children. Yet, inside people's minds, the boundaries of class are still closely drawn. If " middle-class " people have friends, they are usually " middle class " too. There were still two Woodfords in 1959 and few meeting-places between them. It would be interesting to know whether this social structure finds reflection in the prevailing pathology (in, for instance, the extent of incapacity for work and the medical conditions responsible for it); and how far there apply in such a mixed community as Woodford the differences in morbidity with social class found by the Registrar-General to prevail in the country as a whole.

1. Glass, R. Newcomers: The West Indians in London. London, 1960.
2. Young, M., Willmott, P. Family and Kinship in East London. London, 1957.
3. Family and Class in a London Suburb. By P. WILLMOTT and M. YOUNG. London: Routledge and Kegan Paul. 1960. Pp. 187. 21s.
4. Sinclair, Sir John. Analysis of the Statistical Account of Scotland. Edinburgh, 1895.

Special Articles

THE FAMILY'S DOCTOR

A report from the Research Committee of the North Midland Faculty of the College of General Practitioners *

IN many parts of North America and the continent of Europe it is unusual for parents and children to be under the care of the same doctor; and it has been said that, in Britain too, the general practitioner "seldom looks after whole families" [1] and should not be thought of as a family doctor.[2 3] Yet the concept of family doctoring—caring for whole families continuously over a number of years—is cherished by a great many practitioners. They value the relationship with their families, and feel it enables them to provide a better service, especially in respect of infective and psychological illness. Since the advent of the National Health Service in 1948 there has been no financial reason for a British family to divide its allegiance in this respect, and in 1953 reports from two individual practices indicated that 60% and 72% of their patients did indeed constitute whole families.[4 5]

It seemed desirable to collect more evidence, so that discussion of this important aspect of general practice might be based on firmer foundations; and this is a report from six Midland practitioners showing to what extent they were caring for whole households in 1960. They undertook the work primarily as an exercise in research technique, using their own practice records, and the fact that these practices are of very different types is interesting but fortuitous: no attempt was made to choose a sample representative of any larger population.

METHOD

The essence of this survey was the scrutiny by each practitioner of his own records, to see how many of his patients belonged to households entirely under his care.

To avoid unnecessary disturbance of the main files, small duplicate cards carrying the name, address, and date of birth of each patient were made from the medical record envelopes. These were grouped into households on the basis of the doctor's existing knowledge, rearranged later if more information became available, and finally sorted into three categories: "complete households", "incomplete households", and "unknown".

Classification of the records presented problems which were discussed at several meetings as the work progressed. The main difficulty was to define the limits of the "family", especially when some members lived away from home; and it was soon apparent that the "household" was the more appropriate unit for the purpose of this study. A "household" was defined as "all those occupants of a dwelling who keep house (i.e., buy, prepare, and eat their food) as one unit". In using households rather than families, the advice of the Edinburgh workers [6] was followed; but their definition, based on front doors, was rejected. Midland doctors know little of front doors, which they seldom use, but they know a great deal about kitchens and whether these are being shared by more than one housewife.

Surprisingly few households remained unclassified through lack of information. The doctors either knew already, or met during the six months of the survey, at least one member of almost every household in their care. Occasionally a doubtful relationship could be explained by the practice secretary, and it was not found necessary to undertake any extra visiting for the purpose of this study.

Two of the six practitioners examined the records of every patient on their N.H.S. lists. The other four each examined the first hundred records in their files, to see whether any gross difference emerged, and then, after discussion with the statistician, examined samples designed to give statistically satisfactory pictures of their practices. The sampling procedure was based on the figures from the two fully investigated practices and the preliminary surveys of the rest, and it called for examination of at least 800 consecutive records from any part of the alphabetical file. Wherever the doctor knew of the existence in his sample households of persons whose surname differed from the rest and fell outside the sample, he recorded such persons on coloured cards, so that their existence was taken into account in classifying their households, but was not allowed to inflate the sample.

In view of the constantly changing practice populations (estimated by one of the participants as a "turnover" of 10% of his patients each year), this survey, which actually took six months to carry out, was carefully related to a specific date—April 1, 1960. Patients who left the practice were excluded and those who joined were included, up to that date.

MATERIAL

The six practices were identified by the letters A, B, C, D, E, and F.

Practice A lies among the Derbyshire moors. The two partners have their main surgery in a village with 400 inhabitants, and there are four outlying branch surgeries: some patients live as much as fifteen miles from the doctor.

Practice B is more compact, but is also rural, in an agricultural part of Nottinghamshire. One principal and one assistant work from a central surgery in a large village with over 1000 inhabitants: almost all their patients live within a radius of six miles.

Both A and B do their own dispensing, and virtually all their normal midwifery.

Practice C has a rural part in the Derbyshire dales, and extends into a town of 18,000 people. The surgery is at the edge of the built-up area, and is used by the two partners.

Practice D is run by three partners, in a town whose 50,000 inhabitants are chiefly concerned with coalmining and light industry.

Practice E is a town practice in the industrial belt between Derby and Nottingham. There are three partners, but, in contrast to practice D, each attends almost exclusively the patients on his own list. The partner concerned in this study was able to examine his own records as a separate entity.

Practice F is entirely within the city of Sheffield (population 500,000). It is run by a woman doctor working alone, and before the start of the N.H.S. most of her patients were women and children.

None of the last four practices do their own dispensing; and, although they all undertake midwifery, some of their patients make use of the alternative services available. Private practice forms a very small part of the town doctors' work and is negligible in the rural areas.

RESULTS

It was found that 77·4% of the 22,058 people in the care of these six practices have one doctor (or partnership) looking after their household. Such people have a doctor whose knowledge of the whole domestic unit can be called upon when necessary to solve a diagnostic problem in any one of its members.

* The practitioners who took part in this study were D. W. CAMMOCK, E. D. FORSTER, F. H. LEE, AGNES NUTT, G. M. T. TATE, and J. McA. WILLIAMS. The recorder was RUTH CAMMOCK.

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2. Taylor, S. Good General Practice. London, 1954.
3. Titmuss, R. M. Essays on the Welfare State. London, 1958.
4. Backett, E. M., Evans, J. C. G., Shaw, L. A. *Proc. R. Soc. Med.* 1953, 46, 707.
5. Ross, D. R. *Med. World*, February, 1953.
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TABLE I—POPULATIONS OF THE PRACTICES

Practice	a Total N.H.S. patients	b Institution inmates	c Population excluding b	d Sample examined: total, and as % of c*
A	2614	0	2614	2614 (100%)
B	3100	231	2869	2869 (100%)
C	3550	237	3313	1023 (31%)
D	7594	10	7584	800 (10·6%)
E	3422	370	3052	945 (31%)
F	1778	4	1774	797 (45%)
..	22,058	852 (3·9% of a)	..	..

* The institution inmates were excluded from the samples, because their records were not usually in the main files.

Of the other 22·6% of this population, 1·7% belong to households of which the composition was not fully known to the doctor, and 3·9% are resident in institutions—boarding schools, labourers' hostels, old-people's homes, and the like—leaving 17% whose household care is divided between at least two practices.

Table I shows how this population is distributed between the six practices, and the relationship of the samples to the practices from which they were drawn. Table II and the figure show the results obtained in each practice.

A difference between the urban and the rural practices is apparent in these data. It is a real difference, the 5% confidence limits for the proportions in the sampled practices being within ±3% in all cases; but it is not unexpected, since choice of doctor in a rural area is bound to be limited by the number within reach. A more interesting feature of the results is the fact that the three urban practices, different though they are in pattern and organisation, yielded figures so nearly comparable with their rural neighbours and so very similar to each other. Three-quarters of this urban population have one family doctor.

Since the survey unit was the household and not the family it was felt to be desirable to consider, subsequently and as a separate category, all those lodgers, domestic servants, and others whose membership of these households was a business relationship only. If they, as a group, tended to choose a different doctor from the rest of their households, they might form a significant part of the 17% of divided households. In fact only 1% of all the patients were found to come into this category, and of that 1% a third had chosen the same doctor as the rest of their household. So their inclusion has had a negligible effect on the results.

DISCUSSION

Although the study has shown that three-quarters of this population choose to have one general practitioner for their whole household, it has not measured the extent to which the same households use alternative services, such as local-authority clinics, hospital casualty departments, and even private practitioners. Nor has it been possible to examine more fully the 17% whose household care was divided. An obvious reason for the division was known in some cases (as in the Army camp where the men must attend the Army medical officer and their families the local general practitioner); but for many others the reasons could only have been found by direct approach to the patients—a method outside the scope of our investigation.

TABLE II—FINDINGS IN EACH PRACTICE

Practice	Patients in complete households	Patients in divided households	Details unknown
A	2451 (94%)	163 (6·3%)	0 0
B	2553 (89%)	235 (8·2%)	81 (2·8%)
C	(863)* 2784 (84·5%)	(150) 465 (14·6%)	(10) 32 (1%)
D	(608) 5750 (76%)	(173) 1641 (21·6%)	(18) 170 (2·3%)
E	(701) 2260 (74%)	(215) 694 (22·8%)	(27) 87 (2·9%)
F	(574) 1275 (72%)	(220) 489 (27·6%)	(3) 7 (0·4%)
..	17,035 (=77·4% of a)	3687 (=16·6% of a)	377 (=1·7% of a)

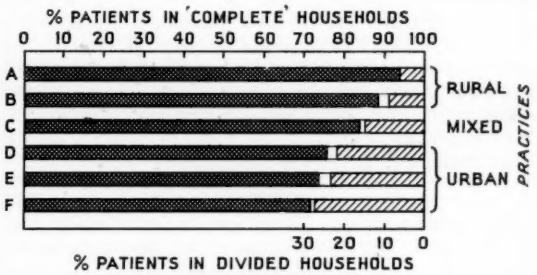
* Figures in parentheses are those actually counted in the samples.

The method used in this study was essentially simple; yet its details, already described, represent the solution of several problems characteristic of research in general practice:

1. The survey unit (in this case the household) had to be practicable. Attempts to use the "family", however defined, produced so many unclassifiable and exceptional cases that the final figures would have had very little meaning.

2. Appropriate sampling technique could only be devised when something was known about the likely range of the results. Once this had been established, by complete examination of two practices, and a preliminary check had shown that the others were not very different, the help of a statistician was essential. With his aid the other four doctors could then plan their tasks to yield results of the desired degree of accuracy without so much labour.

3. Clerical help was of limited use. This work was done most easily by the doctor himself, since he knew most about his patients. The local executive councils could not possibly have obtained this information from their records.



Findings in each practice.

4. The scope of this study was strictly limited. It was thus possible to complete it in eighteen months (from its inception to the presentation of the results) without interfering with the doctors' normal work, and without recourse to any special facilities or funds.

The participants found that the work involved less drudgery and yielded more satisfaction than they had expected. Now some want to look further into the social structure of their practices, to discover the prevalence of three-generation households and of people living alone. Others feel that study of the general practitioner himself should have priority: how often is he a multiple person, and what services does he actually perform? Why do practices differ so greatly? One member of the group is continuing to file his patients' records in households, "because this may well prove valuable in the field of epidemiology". Another, while sorting his patients into households, also completed a register according to age and sex, so that this information will be readily available in future studies. The woman member of the team was pleasantly surprised to find that she is as much a family doctor as her male colleagues.

CONCLUSIONS

Family doctoring, in the sense that the whole household is under the care of one practice, is a reality for over

three-quarters of the population covered by this survey. Previous surveys have not been sufficiently comparable to demonstrate any recent change in this pattern of medical care, and it would seem useful to apply the method of this study to a representative sample of practices at suitable intervals in the future, so that the trend can be observed.

Information about the duration of continuous care—the other important aspect of family doctoring—could be obtained in a similar way.

Much information of this kind exists in the records of all N.H.S. practitioners. It can be collected without any direct approach to patients, and its collection can be a satisfying task for the doctor concerned.

The committee wishes to record its indebtedness to K. W. Cross, PH.D., of the university department of medical statistics at Birmingham, for his advice, help, and encouragement.

HOSPITAL BUILDING PROGRAMME

Mr. Enoch Powell, the Minister of Health, has sent to all hospital authorities his plans for tackling " the immense task of hospital capital development and re-provision as quickly and efficiently as possible ".[1] He believes that the building programme has reached a point where new methods are needed, and he is making administrative changes which will give the boards greater responsibility and allow them to plan further ahead. The maximum cost of projects for which prior ministerial approval is not required is to be raised from £30,000 to £60,000, and he has given the boards tentative figures on which they may base their plans as far ahead as 1966. Under these new conditions he has asked them to submit their proposals before May 31 for work to be started in the next ten years.

The provisional figure for hospital capital expenditure in 1962–63 is £36 million compared with £31 million in 1961–62. According to the provisional figures offered to the boards as guidance in the preparation of their plans, the total expenditure for England and Wales could be expected to rise by 1965–66 to the region of £50 million.

For the first five years the programme will have to be as firm as possible. For the later years it must necessarily be more adaptable and less detailed, and in preparing their proposals for 1966–71 the boards are asked to make an estimate of what is needed and practicable. The Minister intends that they should have freedom to express and justify what they consider to be their reasonable needs, and at this stage they will not be tied to specific financial limits, but they are asked to take into account their probable resources of staff and running costs.

Changes which will affect the more immediate future will be the publication by the Ministry of a series of *Building Notes* giving guidance on planning and design, and the introduction of a system of cost limits which will obviate detailed examination of plans which conform in design and cost to the suggestions made in the notes. It is also proposed to move as soon as possible to a system whereby a date for the actual start of a building will be given at the time when the scheme is approved.

The first *Building Note*,[2] which was published a few days after the Minister's announcement, gives guidance on the drawing up of long-term plans.

The need for beds of different kinds will vary according to local conditions, but as a general rule it is suggested that per 1000 population not more than 3 acute beds, 1·2 chronic-sick beds, and 3·5 mental-hospital beds will be needed. (This last figure is expected to fall perhaps by half within the next fifteen years.) Maternity beds should be related to estimated births and not to population and should follow the Cranbrook recommendations.

The general hospital of the future, it is further suggested, should contain inpatient beds and treatment and diagnostic facilities for inpatients and outpatients, including a maternity unit and an acute psychiatric unit, a geriatric unit, and an isolation unit for patients with infectious diseases. Planning must aim at flexibility to meet the needs of new medical techniques and treatments, and avoid a rigid allocation between specialties and between the sexes. There is likely to be an increasing demand for some forms of pathological investigations; greater emphasis on the grouping of inpatients according to their nursing needs; greater use of hostel beds for patients who are able to fend for themselves (e.g., those patients having radiotherapy treatment); and provision for day patients in outpatient departments. A hospital should be located in the town that it serves rather than outside it, and, though ideally a hospital of 600 beds needs a site of about 30 acres, in urban areas a much smaller site may have to be used.

1. H.M. (61) 4.
2. Buildings for the Hospital Service. Building Note no. 1. H.M. Stationery Office. Pp. 8. 1s. 6d.

Medicine and the Law

Suffocation from Plastic

AT an inquest at Honington R.A.F. station on Jan. 19, the deputy coroner recorded a verdict of " death by misadventure " on a month-old baby boy suffocated in a carry-cot with a plastic-covered mattress.[1]

The mother stated that she had placed the baby in the carry-cot with a small pillow. As he was crying, she turned him from his back to his side and tucked him up. When she returned he was " blackish " in colour and dead, lying face downwards on the mattress, with his head under the pillow. A pathologist said that necropsy revealed asphyxia as the cause of death, with respiratory infection as a probable contributory cause. The jury expressed the view that plastic-covered pillows and mattresses were not suitable for babies.

Public Health

Respiratory Infections

THERE were 246 deaths attributed to influenza in the week ended Jan. 14. 225 of those who died were 55 or over, and 119 were over 74. 185 of the deaths were in the Midlands and the North-west. The disease is becoming less prevalent in north Birmingham and north Warwickshire, but not in the south of the city and county. In Lancashire, there is a severe outbreak in Preston.[2] London, south-east England, and Wales remain comparatively free. Only 3 of the deaths were reported from the administrative county of London.

Vital Statistics for 1960

Provisional figures of the main vital statistics for England and Wales for 1960 have been issued by the Registrar General.[3] The birth-rate was 17·1 per 1000 population—the highest rate since 1948. The death-rate was 11·5 per 1000 population (11·6 in 1959). The infant-mortality rate was 21·7 per 1000 live births (22·2 in 1959). The excess of births over deaths registered in 1960 was 256,395—the biggest excess since 1948 when it was 307,072. The stillbirth-rate was 19·7 per 1000 total live and still births (21·0 in 1959).

1. *East Anglian Times*, Jan. 20, 1961.
2. *Times*, Jan. 23, 1961.
3. Registrar General's weekly return no. 2, 1961. H.M. Stationery Office. 1s. 9d.

Symposium

RESPONSIBILITY IN HOSPITALS

WITH Lord COHEN OF BIRKENHEAD presiding, a symposium was held on Nov. 4 by the Newcastle Regional Hospital Board. Mr. E. F. COLLINGWOOD, chairman of the board, explained that its theme was responsibility for patients—the responsibility of doctors and of other members of the hospital organisation.

OPENING REVIEW

Dr. T. F. Fox said that, though the hospital is the medical equivalent of the factory, in our Industrial Revolution we have so far preserved the old principle of personal care: the patient is transferred from his doctor at home to an individual doctor in hospital, who is supposed to accept full responsibility for him. But this system no longer works as well as it did. More and more, the consultant sees himself as an expert whose beds exist for the practice of particular techniques; and this can be harmful, because so many patients have more than one disorder, and their reaching one expert rather than another is sometimes a matter of chance. The person who should know the patient best—his home doctor—is seldom in the hospital picture at all.

As to what might be done, Dr. Fox quoted some suggestions made to him by Dr. Thomas Dormandy. Regarding " watertight " firms as outmoded and inefficient, Dormandy argued that " in a modern hospital a physician should routinely see every surgical patient; radiologists and pathologists could with advantage do routine rounds in every ward; no accident case should be left in the orthopædic unit without being seen at least by a neurosurgeon; and psychiatrists could be more than the dead-end posts for patients who have already been around every other department ". Instead, the large hospital should be organised in more or less close units, each providing for every (or almost every) specialty.

" To me ", said Dr. Fox, " this sounds good sense, though often hard to apply. I would like to see some hospitals try much larger firms or units, in which some of the senior people, though they continued to use various expert skills, would depute the care and handling of the patients to younger men. The person who was taking charge of the patient must, I think, be a consultant; but he ought to do rounds at least once a day. He would have to see that the full resources of the unit were deployed wherever useful; that time wasn't wasted; and that on discharge an answer was given to ' the question implied by the patient's admission '. Where necessary he must set in motion the wheels of rehabilitation, resettlement, and social welfare.

" Who did this work would partly depend on who wanted to do it. I should suppose that very often, if not normally, the doctor appointed by the unit to have charge of patients would be a young physician. He would not have particular beds permanently, but his name would be on the bed of whatever patient he undertook. In one sense he would be in charge of the patients more completely than most consultants today; for he would accept a closer responsibility, becoming the patient's own doctor in hospital. On the other hand, he would sometimes have to defer to the opinion of seniors in his unit, and he would thus be acting with the delegated authority of that group rather than by his own divine right.

" How could the unit exert its influence while still leaving the doctor free and responsible—which means free to make mistakes? The answer, I think, is that control should be retrospective. A unit can properly influence its members by meeting periodically to review retrospectively all admissions and discharges."

To ensure that everything necessary is done, the doctor assuming responsibility must keep in touch not only with the patient every day but with the specialised or senior members of his group, with the relatives, and (not least) with the home doctor.

" Nothing quite excuses sending patients out without explaining things fully to their home doctors: it is really a professional crime. Personally, I think that all local practitioners who are prepared to cooperate with the hospital by sending proper notes should be made associate members of the staff; they should have a common room where they can meet consultants, and they should visit the wards as of right. But I think we should also follow the practice of the Massachusetts General Hospital, where housemen are urged to telephone to the patient's doctor, whatever the distance, if they want information, and in any event when the patient is going out."

James Spence said that what matters in the National Health Service is not the service, which is an abstract concept, but the institutions, large and small, which actually cope with patients. The institutions, again, depend on the people composing them; and here we must pin our hopes on more and more of these people having a professional attitude. No administration can devise a system without any gaps; but if everyone feels responsibility for the institution as a whole, then even a highly deficient staff can make the thing work.

"Nevertheless, our system ought not to call on people to hold posts in which they are uncomfortable, through lack of knowledge or experience. Nowadays, as we all know, the responsibility placed on housemen and casualty officers is often far too great. One way of overcoming this evil is that seniors shall be ready and willing to guide and assist, regardless of their status; but another is that we should cease to ask institutions to do work that is really beyond them. Early revision of arrangements for treating accidents is an urgent case in point."

Much of the responsibility for what goes on in hospitals doctors must share with administrators; " but I am clear that, even if we accept the legal view that patients are ultimately under the care of the hospital as a whole rather than of any group or individual, responsibility for the patients should still be delegated to one medical person. And I think we should be careful not to weaken that responsibility, once conferred on him ". Perhaps the main objection to the present system is that the person in charge is too often a specialist, in whose bed the patient too often lacks good general care.

THE LEGAL SIDE

Dr. S. COCHRANE SHANKS (president of the Medical Defence Union) said that under the legal doctrine of *respondeat superior* the hospital authority is now responsible for the negligent acts of its staff, be they medical, nursing, ancillary, or lay. The authority has, of course, a remedy against its staff: if it is sued, it can join them in the action or it may seek contribution from them afterwards, if damages are awarded against them.

" I am glad to say that it is settled policy now in the hospital service that no contribution will be sought from the nursing, the ancillary, or the lay staffs . . But the doctor is in a different position; indeed, in the beginning of the National Health Service, the Treasury issued instructions to hospitals that they should seek contribution from a doctor, or join him in an action, if he was the person primarily responsible for negligence for which the hospital was sued. That created considerable difficulty at first . . . and so, after prolonged negotiations between the defence societies, the British Medical Association, and the Ministry of Health, we have come to an agreement, embodied in H.M. (54) 32 . . . by which hospital and doctor will

never fight each other in open court. They will either fight it together, or settle it together, or allow one to settle on behalf of both. In regard to the payment of damages they will agree the percentage to be paid by each and failing agreement they will each pay 50%."

As a member of a learned profession, the doctor is personally responsible for his acts of negligence. The defence societies recognise this, and are prepared to stand behind their members in case of alleged negligence—either to fight, if they regard the complaint as unjustified, or to settle, if the claim is just. The agreement with the Ministry obviously relates only to those who are members of a defence society, and hospital authorities should make it a condition of employment that a doctor should be a member of such a society and should continue to be so throughout his term of office—ideally for three years after, but that might be a little difficult to achieve.

In the hospital service, if the instruction given by a senior to a junior or subordinate is wrong, he may be found legally liable for their errors but not otherwise. In private practice, however, where the doctor is the employer of a nurse or assistant, even if his instructions were accurate, the fact that he put his assistants in a position to do the negligent act is enough, and he must take the consequences.

After referring to the Ministry of Health's memorandum, agreed with the professional organisations, asking the medical staffs of hospitals to try to prevent harm to patients resulting from the physical or mental disability of their colleagues,[1] Dr. Shanks concluded by saying that we should be thankful that our defence societies have two purposes. "They are not only ready to defend the interests of doctors, but equally ready to meet the just claims of those who so trustingly place their lives in our hands."

ADMINISTRATION AND OUTLOOK

Prof. E. A. PASK (chairman of medical advisory committee, Royal Victoria Infirmary) was not hopeful about the administrative approach to responsibility; but he thought that, provided the economic situation allows them to do so, doctors will probably do the right thing. They have no inclination to go off into lonely autonomous action, provided they have the chance to collaborate.

"We must decide, therefore, how high we are going to set our sights, and how much we are willing to pay for medicine; indeed, the administrative rearrangement that Dr. Fox outlined would clearly be very much more costly than anything that exists at the moment. If we are willing to pay that extra cost for medicine, I personally think that we could to a large extent let things run naturally. Given the opportunity to consult with one another, I do not think that doctors are reluctant to do it.

"The control mechanisms for review, for retrospective examination, for the stimulation of new work, develop naturally in the medical hospital organisation. The trouble with meetings, clinicopathological conferences, and so on, is that people have not time to go to them. If they had time they would be there, by nature and instinct, and if you try to introduce administrative changes, to coerce people so to speak (I use this in a broad sense) into particular channels, then you run the risk of attacking necessary autonomy.

"In other words," said Professor Pask, "I feel strongly that the problem is one of opportunity, and then the natural development of mechanisms of which doctors, at any rate, are rather fond. Finally, of course, it comes back to teaching." If the younger men do not have a professional attitude, then it is largely the fault of their teachers.

1. Circular H.M. (60) 45; see *Lancet*, 1960, i, 1255.

Prof. MARTIN ROTH (King's College, Newcastle) pointed out that specialisation has brought untold benefits but also certain disadvantages to which we have not yet adjusted. Not only does it isolate patients for study by special techniques, but it also isolates doctors working in that field, leading them to place too high a value on their own department. It tends to foster possessiveness on the one hand and a buck-passing attitude on the other.

With an ageing population "we are all geriatricians now", and in geriatric medicine one cannot make hard and fast divisions either between different organs of the body or between the body and the mind; diseases tend to have a nebulous, diffuse, indefinable quality which makes them difficult to deal with under any one specialty.

The only antidotes to specialisation are improvements in cooperation, in consultation, and in information; and Dr. Roth was less confident than Dr. Pask about the ease with which these can be achieved at present. He regarded our systems—medical, nursing, and administrative—as too hierarchical. Often the hospital consultant who has responsibility is not there long enough to establish an adequate relationship with his patient. The person who is there a lot of the time is junior, and he may have neither the experience nor the responsibility; "and this, it seems to me, is the situation which we have to remedy". Much of medicine is coming to be a war of attrition against disorders that are long and sustained; and if the doctor does not establish an effective doctor-patient relationship—if he allows depersonalisation in the patient—he will fail in his task.

Administrative arrangements can help, but they require some fundamental alterations in outlook. Having taken two steps back, we now need to take one step forward. The two steps back are the steps taken when treatment moved from home into hospital. The step forward is to relearn something about the social and psychological aspects of illness. "With the very best administrative arrangements, we shall not get any further until we have done more to teach these aspects of illness to students, to physicians, to surgeons, to administrators, and to nurses."

THE HIERARCHY

Asked to discuss Professor Roth's assertion that there is too great a hierarchy in the structure of medicine, Dr. COCHRANE SHANKS said that in radiology one senior has to be responsible for the general organisation; but the director of a big X-ray department must surely leave his colleagues unfettered clinical responsibility, and in that respect he was against the hierarchy system. It used to flourish in Scotland: at the Glasgow Royal Infirmary there were six surgical chiefs, and a host of juniors who had no beds and had to do pretty well what the chief told them. If tried at University College Hospital, this system would blow the roof off in about a week!

Professor PASK thought that the alternative to some form of hierarchy was the endless committee meeting—of which he was equally nervous. He believed that the fundamental need is not to try to arrange medical people in particular patterns; the fundamental need is to give them enough time and allow them to arrange their own pattern. Most of the criticisms of the actions of consultants arise from their not having enough time or enough help. If they had, they would do the job.

Mr. GILBERT PARKER (orthopædic surgeon, Middlesbrough) remarked that consultants do intend doing all the

things they ought to do, but life is very short. Every consultant ought to have his own private secretary to keep him up to scratch. Instead, he was offered a share in a pool of typists, or even a tape-recorder.

Professor ROTH admitted having oversimplified his presentation. He had been thinking particularly of psychiatry, where it is inevitable that one person is in charge of each patient; for example, if a registrar is deputed to look after a patient, then it disrupts this relationship for the consultant to interfere in it excessively. The consultant can give directions and advice only in very general terms, the registrar being responsible for the daily care of the patient throughout his stay in hospital. In surgery this has all sorts of perils; but he believed that some better substitute can be found, even in medical and surgical departments, for the present rather rigid hierarchical structure. More notice could usefully be taken of what has been done in investigating the effect of certain administrative structures on the life of hospitals. What has been found to matter—in mental hospitals certainly—is the quality of the leadership at the top. As head of the unit a person of greater experience is obviously needed, with a role suited to his level of experience. But in a system which is fundamentally undemocratic the quality of the autocracy at the top goes all the way down to the bottom and impinges upon the patients.

SUPERINTENDENTS

Speaking of departmental actions that can cause upheaval, Professor PASK had referred to "the contribution to efficient coherence in a hospital that can be made by a senior medical administrator", and discussion arose on the advantages of having in each institution a medical superintendent:

Professor ROTH thought that in psychiatric hospitals the superintendent has a very important function: he has a major part in ensuring that the therapeutic atmosphere is correct. The time has not yet come when the sort of lay administrative structure that has grown up in general hospitals can be provided in psychiatric hospitals.

Professor Pask explained that he firmly believes that the doctors should run hospitals. If they want to run them through a purely lay administration, the medical staff committee must be willing to meet three times a week for a couple of hours in the evening, because problems arise in this way. As this is obviously impossible, one gets to the third position—that when someone intends to do something, he reports it and discusses it with somebody who will at any rate broadly understand what it is all about. The probabilities of conflict are thereby reduced.

Dr. W. A. NICHOLSON (physician, Hartlepools) said that in his area they have "medical liaison officers", who are elected by the medical advisory committee and are therefore removable. To them other members of the staff say what they want to do, and the liaison officer takes it through the house committees. "On the whole I think it seems to work fairly well, and it is a way round the medical superintendent, which somehow is a nasty word in general hospitals."

Dr. G. MCCOULL (medical superintendent, Prudhoe and Monkton Hospital) said that some years ago he wondered whether he was one of those autocrats people wrote to *The Lancet* about. But he sometimes felt that the total potential collective responsibility in any group is (at the personal responsibility level) that of its weakest member. He doubted the contrast between individual and collective responsibility.

SUCCESS AND FAILURES

Mr. P. H. CONSTABLE (house-governor, St. George's Hospital, London) said that to see that a hospital is giving the best performance that it can with the resources and the money made available to it is an immense responsibility. Following American example, some independent body—the Nuffield Trust or the King's Fund—might set up a small body to see whether we cannot arrive at some qualitative estimate of our performance. "I believe that in the course of doing that we should come upon many of these responsibilities, and many of these failures in co-ordination. We might even come upon the means, here and there, of putting them right."

On responsibility to the patient, Mr. Constable spoke of Dr. Lipscomb's paper on Seeing the Patient Through.[2]

"The patient comes to outpatients, and is seen by this young doctor, maybe a house-officer, a young registrar, a senior registrar, consultant; he goes to a radiologist, he goes to a pathologist, he gets more reports; he goes away at that stage; there is very likely no letter sent to his own doctor; he does not go and see him—he comes back to a succession of doctors." The result is what Lipscomb called the "birds of passage syndrome".

Mr. Constable himself thought that there is "failure in many cases in the end of our performance; most excellent medical and nursing care is given, but the whole thing is not always rounded off as a complete treatment for the patient". The way to success in management in hospitals is that the best possible people, with experience and personal quality, should be chosen as the most senior officers—medical, nursing, and lay—and that these officers in turn should take a lot of care in choosing and nourishing and preserving the heads of their departments. "Then this responsibility will flow right down the line."

CHANGING RESPONSIBILITIES: INFECTION

Dr. R. BLOWERS (Public Health Laboratory Service, Middlesbrough) said that in practice things may go wrong for one or both of two main reasons: (1) that those who perform a task may not perform it with a proper sense of responsibility, and (2) that responsibility for that task may not be in the right place. In investigating outbreaks of infection, he sees no lack of the sense of responsibility: it is remarkable how often physicians and surgeons draw attention to faults in their own methods; how much time they give to studies of these methods; and how quickly they apply an improved technique, even if it causes them a great deal of trouble. In Dr. Blowers' view, the common faults of hospital routine that seem to cause infection occur more often because, for some tasks, the established chain of responsibility is no longer the right one.

Common criticism of the present system is that those who have to work in the hospitals are not allowed to decide on the design or to select major equipment. Is this a legitimate complaint? Except sometimes in the heat of the moment Dr. Blowers thought not: "The solutions to some of the problems of design are so far removed from the obvious that few of us, faced with them for the first time, will make the right decision; and few of us are involved in the building of more than one or perhaps two hospitals." But this does not mean that no change in the present system is needed.

"There is at least one grave fault. When local advice on matters of design is rejected, the senior medical staff who gave it often cannot find out whether it was rejected by an officer of a regional board, whether it was rejected by the board itself, or by the Ministry of Health. If we in the hospitals are to be responsible for making the place work, after others have been responsible for building it—if this mutual sharing of responsibility is to work—each side must know who the other side is."

2. Lipscomb, J. M. *Lancet*, 1949, ii, 495.

As regards sterilisation, the Nuffield Provincial Hospitals Trust pointed out that in some hospitals nobody is responsible. Clearly somebody should be responsible, but who?

"Whoever takes on the job—the surgeon, the pathologist, or the engineer—has got a to do lot of homework before he can start. He must learn a lot of the work of the other two. But, as I see it, an operating-theatre is a surgical department, and only a surgeon can be responsible for running it, and he is the man to be responsible for the sterilisers in it. If the dressing steriliser is somewhere else, down in the basement, I would still regard it as a detached part of the theatre. If, of course, it becomes part of a central sterilising department, with its own supervisor, then we have a different state of affairs. Often the responsibility for sterilisation falls on a pathologist; if he is willing, all well and good, but I do not think that this can be demanded of him; if he cannot take it on, I do not see how the surgeon can avoid the responsibility. I was once astonished to hear a surgeon say, 'I expect sterile materials, but surely no-one expects me to know how they are sterilised?' A bacteriologist might equally say, 'I want sterile culture media, but how they are made is no business of mine.'"

This is a matter for which responsibility often bears on the wrong shoulders or rests nowhere at all; and Dr. Blowers thought we should urgently see that it finds its proper place. Here there is room for experiment.

"Changes of responsibility are often resented, and the people from whom responsibility is taken have sometimes refused to have it back when the new system does not work. But surely, if there are possible advantages in a change, we should investigate its value, not only in theory but also in practice. After all, we are prepared to do this for new methods of medical treatment, and I see no reason why we should not accept research in responsibility, just as we accept it for the more scientific parts of medicine."

Mr. W. T. WING (group pharmacist, Newcastle upon Tyne H.M.C.) said that pharmacists already supply a substantial amount of sterile material for parenteral medication, and could, if it was felt desirable, undertake the preparation of sterile dressings—work for which their training prepares them. In this way pharmacists might relieve other staffs and perhaps enable them to give more attention to the patient.

Dr. P. C. YOUNG, in an account of the work of the British Standards Institution of which he is divisional chief technical officer, said that among more than 3000 British Standards more than 200 have been designed specifically for hospitals.

The policy or advisory bodies include the Hospital Equipment Standards Advisory Committee, the Surgical Instruments and Medical Appliances Industry Standards Committee, the Dental Industry Standards Committee, and the Ophthalmic Standards Committee; but many other committees also produce and assist in the preparation of British Standards of interest to medicine.

NON-MEDICAL COLLEAGUES

Dr. E. G. BREWIS (pædiatrician, Newcastle) said that everything affecting the wellbeing of his patient is the consultant's personal concern, in greater or lesser degree. Too often, he thought, senior medical staff consider that anything outside diagnosis and treatment is of no account, or belongs to some other department. He regarded the non-medical staff as colleagues without whom the medical staff cannot work, and who themselves cannot function properly without the cooperation and guidance of doctors. The occasional tendency of staff to consider that they are there for their own sakes, and their departments are sufficient unto themselves, may be dispelled by the simple statement that without the patient the hospital is meaningless.

The closest associate of a doctor in treating his patient is the nurse: she spends much more time than he does in observing the patient, and without her he can really do very little. One of the most important responsibilities of the doctor towards the nursing staff is to keep his demands of them within the limits of their training and capabilities. Too often, through shortage of junior medical staff, nurses are asked to carry out techniques and supervise treatments far beyond what is reasonable. It is also important to achieve the best working conditions for the nurse. Many consultants hardly know what goes on in the back rooms of their wards at all, and the type of weekly ward inspection which obtained in the Navy had much to commend it.

Particularly is this important as regards the prevention of infection, the principles of which seem so difficult of acceptance by both doctors and nurses. Here again, free explanation and discussion are invaluable, and, perhaps above all, rigid adherence to the rules by the medical staff, who are often the most blatant offenders. Discipline must be exacted from all personnel, including maids, porters, and cleaners, in the interests of the safety of patients and staff alike. It is also the doctor's responsibility to take part in the training of nurses, and to make sure that the things taught in the preliminary training school are standard practice on the wards. He must contribute, too, by giving lectures to nurses, and when possible by helping in ward instruction.

On the other side the non-medical staffs have a responsibility to the doctors, who are entitled to, and usually receive, their very close cooperation. From the nurses, absolute loyalty is demanded in carrying out all medical treatment, whether the rationale is immediately apparent or not.

For doctors to give attention to the work of the many different kinds of staff in the hospital, it might seem that they have got to be supermen or they have got to be dedicated. In point of fact most of these things can be done in the ordinary course of one's daily work—but more easily in a small hospital, where personal contacts are frequent. It is through personal contact that most things get done, not only in hospital but in any other communal enterprise.

MATRON AND SISTER

Miss F. SHAW (matron, Royal Victoria Infirmary) said that the average matron in this country is carrying an unbearable responsibility.

In a regional hospital, between 5 P.M. and 9 A.M., apart from the medical care of the patients, she is not only responsible for the nursing staff, but she or her deputy has to be at hand to ensure that the dispensary services are adequate, that the laundry and the linen will be sufficient, that the domestic staff coverage is sufficient, that the electricians can be called in to deal with any fault, and even that action is taken if there is an emergency over the plumbing. Shorter hours—in the laundry for example—are helping to make this situation even more difficult: there seems to be a tendency to give better working conditions to the ancillary staff and to leave the matron to work out the consequences.

After the care of the patient, the matron's greatest responsibility is to the student nurse and to her ward sisters:

"I think that if more senior tuition was given to members of the nursing profession after they had finished their initial training, then a great deal of the matron's problems would be solved. For instance, after being a student nurse, in the majority of hospitals she rises by virtue of service, and good testimonials, to become a staff nurse. If that hospital is desperately short of staff, she may not even have a good testimonial; she may just be someone who will be a pair of hands. We want a great deal more help in the nursing profession with courses of training for the ward sisters and senior administrators . . . It is becoming

increasingly difficult, if not impossible, in some areas to appoint senior nursing staff of the right calibre."

What is needed to enable ward sisters to carry their tremendous responsibility is more help for the sister herself—clerical staff, more staff nurses, and various centralised systems. Without these, nurses will not be able to accept their proper responsibility, because of the trivialities with which they are constantly involved.

A "PATIENT'S FRIEND"?

In his opening paper Dr. Fox had pointed out that anxious patients and their relatives need explanations and comfort from someone: if the ward sister was too preoccupied by other tasks, was there not a strong case for a receptionist or patient's friend, who could help sister and the doctors with this side of their work?

Dr. R. G. RUSSELL (chairman, Hartlepools H.M.C.) said that, in the casualty department at Hartlepool, a friendly lady, dressed in a pink coat, has been employed as receptionist, and this has been quite successful.

Miss SHAW could not suppose that a "patient's friend" is the right solution. For the sister herself would have to tell the "friend" about the relationship between patient and doctor, and the whole details.

Dr. NICHOLSON thought that, even in a big ward, the sister could do this work, if not overburdened with unnecessary tasks like going over linen stock once a month.

Miss C. M. HARKER (matron, Friarage Hospital, Northallerton) was against the introduction of any third person between the sister and the patient or relatives. This would take away one of the sister's most important duties. If she was so harassed that she could not have proper contact with her patients, she ought to have more staff.

Professor PASK was unhappy about administrative moves which tend to economise. To accept them was to say that we must aim a bit lower than before. In commenting on the discussion, Dr. Fox agreed. We must somehow enable all sisters to do the work that they should be doing—either by giving them more staff or perhaps by getting them to look after fewer people. In new hospitals the size of wards should be decided not by convenience of plumbing but by the number of people a sister can properly look after.

TELLING THE PATIENT: WHO, WHEN, WHAT?

Dr. ANDREW SMITH (chairman, N.E. England faculty, College of General Practitioners) said that the hospital's responsibility does not end until the family doctor knows about the diagnosis, treatment, and prognosis. (The delay is often astonishing; but, in contrast, one department at the Royal Victoria Infirmary telephones practitioners on the night their patient is discharged.) What the patient and his relatives especially want to know is the outlook; and tremendous damage can be done by a wrong prognosis. Where the prognosis is bad, it should generally be given by the family doctor; sometimes by the consultant but never by a houseman.

Mr. D. A. SANFORD (surgeon, Sunderland) thought that the consultant should talk to the relatives; it is in his own interests to do so, because the patient who has a bad prognosis, leaves hospital without the relatives being told, and then goes downhill is the beginning of litigation. So, in his own defence, he would not delegate this to the general practitioner or anybody else, if he had time to do it. But in his experience it proved to be a five-day-a-week job, at seven o'clock in the evening, for an hour. "I am not a hero and I gave it up."

Mr. D. C. DICKSON (surgeon, Middlesbrough)—who regarded the whole symposium as an example of taking a steam hammer to break an egg—pointed out that many patients do not want to know too much. The doctor's responsibility is to say "I will put you right" (or "I will try to") without too much explanation. It is humbling to remember that one can talk to one's patients and see them every day—yet five years later they do not know who did the operation. "If we sell ourselves properly to the patient, they will accept our responsibility."

Dr. T. E. HURLEY (regional psychiatrist, Newcastle R.H.B.) recalled the eminent surgeon who always said that he told the patient everything. He used to examine the patient and then say: "Now look, there's something wrong inside. We'll take you in and cut the bad out"!

Dr. G. D. OWEN (physician, Darlington) pointed out that it is not the diagnosis that is important but the impact of that diagnosis on the patient and his family circle. At times of exasperation one may feel that the less they are told the better. Yet an extremely sound general practitioner told him that one of the great advantages of securing a 45–60 minute interview with the consultant, by sending patients to him privately, was that they came away with a reasonably clear idea of what was wrong with them. How are we going to apply those standards to the hospital service?

PERSONAL CARE IN CHILDREN'S HOSPITALS AND OBSTETRIC HOSPITALS

Dr. GEORGE DAVISON (pædiatrician, Newcastle) said that for some twenty years children's hospitals had been trying to give the kind of care suggested. "We have been preaching that a sick child is a sick child—not a medical, surgical, or other special type of patient." In Dr. Davison's view the pædiatrician (he does not like the word) is a kind of general practitioner, working in hospital, whose duty is to look after the welfare of all the children in his wards, while the technical and the specialist care is in the hands of the surgeons or other specialists. Pædiatrician and specialist consult together, but the pædiatrician is responsible for the general welfare. There are frictions, of course: "but in at least one hospital in this area it does work."

Prof. H. HARVEY EVERS (pastoral visitor, Newcastle R.H.B.) said that obstetricians have the good fortune mostly to work in smallish hospitals, which makes for a personal approach. Midwifery provides an excellent example of cooperation of doctors with each other and with nurses and other members of the team. If some of the larger institutions were able to model themselves on the smaller, it might possibly be to everyone's advantage.

COLLECTIVE IRRESPONSIBILITY

Mr. T. G. LOWDEN (surgeon, Sunderland) told the story of Cinderella:

> Once upon a time, Cinderella cut her eye, and the Ugly Sisters took her to the Eye Hospital. At the Eye Hospital they said "My dear, you have not cut your eye; you have cut your eyebrow. This is an Eye Hospital, not an Eyebrow Hospital; you will have to go to the Accident Hospital, you poor little thing." At the Accident Hospital they X-rayed Cinderella's skull. They looked at the X-ray and they said "No bony injury. N.A.D. You should be at the Infirmary, you poor little thing." So she went to the Infirmary, and at the Infirmary they looked at her and they said, "But this is a child. You should really be at the Children's Hospital, you poor little thing." So at the Children's Hospital they took her in, and transferred her to the Plastic Unit, which was many miles away; and the Plastic Unit sewed her eye up, and they did it, as they do, very very beautifully.

Now each of these doctors, at each of these hospitals, individually thought he was doing the right thing. Nobody was responsible, because everybody was responsible. The

relationship between the responsibility of one specialty and the responsibility of all the other specialties is, said Mr. Lowden, particularly vulnerable in dealing with emergency cases. With routine cases and list work, surgeons can be left to develop their own methods, and stew in their own juice; but in urgent cases " with a variety of hospitals, a multiplicity of specialties, a constantly changing population of juniors and residents, and a United Nations from which to recruit them, there are ever-increasing dangers of losing our patients in the confusion; there are ever-increasing opportunities of passing the buck ".

CASUALTY DEPARTMENTS

Mr. B. S. BRARA (surgical registrar, Sunderland) said that the casualty officer's main problem is that of head injuries. If an observation ward with two or three beds were attached to the casualty department, it could be a great help. He thought, too, that in the peripheral hospitals, wherever possible, the accident service and the neurosurgeons should be near each other.

Prof. A. G. R. LOWDON (dean of medicine, King's College) also spoke of the enormous responsibility borne by the young men put in the casualty department. " I do not see any solution for this, except that every patient who needs to be admitted for observation should be able to have a bed. I do sympathise greatly with these young men who are asked to take the responsibility, sometimes, of refusing admission for a patient, because the shortage of beds is so great."

THE TEACHER'S RESPONSIBILITY

Professor Lowdon, in his main speech, talked about the importance of teaching the younger people—not just in a medical school but everywhere—young doctors, young nurses, or orderlies in hospitals. All these people must be taught a lot about fact, about what must be done and what must not be done; but they must also be taught an attitude. He distinguished responsibility *to* the patient from responsibility *for* the patient. Doctors and nurses are mostly concerned with the first, and this is a thing that in a teaching school must be kept in the forefront.

" I sometimes feel a little despondent because, although we can teach it, it is to a large extent a thing that is inborn in individuals. They really either do have enough sympathy with their human fellows, or not, to be good doctors. I sometimes wonder whether, at the end of a medical curriculum, we should not choose those who have shown themselves not to have this sympathy, or this empathy, and direct them into laboratory work instead of clinical work. There are, of course, those who share no less of the responsibility, but who are not directly connected with the patient, those who share the responsibility *for* the patient, and these I think we must teach the sense of responsibility, about which so much has been said."

However much this is taught by statement of fact, the attitude is what matters most.

" It is the enthusiasm of the senior people, their own sense of responsibility to the patient and for the patient, which finally gets this across . . . It is not good enough for the senior clinicians to feel that, just because they are senior, they may hurry round the ward at the bottoms of the beds, and be rather impersonal, leaving if for the younger men, who have more time, to be more personal. I am not sure that the senior people should not delegate more of their clinical responsibility . . . and be more personally intensively responsible for a few patients, in order to treat these patients properly, and to show the right example to their young people. Maybe we are all a little guilty of trying to do too much, instead of trying to do a little really well, and give the best example to our younger colleagues in responsibility.

Mr. LINTON SNAITH (obstetrician and gynæcologist, Newcastle) underlined Professor Lowdon's comment by saying that every hospital is a teaching hospital, and also that the clinical head of the team must, somehow, be able to concentrate his work, as an example to juniors.

Mr. DICKSON thought there ought to be some way of exercising economic pressure on the " bad boy " in the hospital service—the man who was the cause of this symposium, by and large. Some senior member of the medical staff ought to be able, in the last resort, to say: " If you do this again I will report you to the regional board, which will dock your salary ". This is something that needs to be considered because there will soon be no more teachers who were in the service of the old voluntary hospitals.

Prof. NORMAN HODGSON (pastoral visitor, Newcastle R.H.B.) wholeheartedly supported Professor Roth and Professor Lowdon in saying that the tone of the clinic depends upon the example set by the head of that clinic. But, being responsible for his juniors, he must not, if they are unsuitable, let them go on until they have reached the point of no return. They should be told early and guided into other work. Secondly Professor Hodgson was quite sure that the place to learn how to treat patients, and how to treat relatives, is general practice. The young doctor, he thought, should spend his preregistration year in general practice, and then start his hospital work.

Mr. SANFORD said that, though teaching starts in teaching school, much could be done to continue the education of people already in the hospital service. The only danger is that " if you lecture to people who already want to do something, and do not provide them with the money and the time to do it, you are likely to produce the opposite reaction to the one you intended! "

Mr. COLLINGWOOD, in his concluding remarks, said that the board had arranged the discussion " not, if I may say so, for the reason that Mr. Dickson advanced, that there are ' bad boys ', but because there are real problems, which arise from the sheer increase in the weight and complexity of the organisations that we have to handle. Changes in the distribution of responsibility are inevitable, and they tend to lag behind the realities."

TEACHING HOSPITALS AND OTHERS

Mr. R. S. VENTERS (chairman, Special Area Committee, Newcastle R.H.B.) suggested that many of the faults of teaching hospitals do not wholly apply to peripheral hospitals. The greatest amount of medicine is done outside the teaching hospitals; and in the smaller peripheral ones there is unquestionably a much more personal attitude towards the patient. There is also more consultation between consultants. Teaching hospitals, Mr. Venters felt, are too big, and new graduates would often be well advised to look for house-posts in the peripheral hospitals.

Mr. Venters also pointed out that, now that more work is done in the peripheral hospitals, the cases sent to teaching hospitals are mostly those that present difficulties. Yet in his experience, when difficult cases are sent to the teaching hospital, they are lost. " Nobody writes to us or tells us what has happened to them."

GENERAL PRACTITIONER, HOSPITAL, AND LOCAL AUTHORITY

Mr. SNAITH wondered whether the real solution to many of these problems is not going to come somehow from the general practitioner coming in to the hospital; because ultimately he is, or should be, the one who carries responsibility for coordinating, for finalising, treatment, and often for carrying information to relatives. Perhaps the two halves of medicine could be intermarried by relieving the practitioner of some of his load, so that he has more time to come into hospital.

Dr. ANDREW SMITH: "That is, of course, the answer." As Dr. Fox suggested, all general practitioners who are willing to supply information about their patients could be made associate members of the hospital staff. If they come in and talk to their own patients in the hospital, they do not need to be given letters when the patients are discharged.

Dr. J. B. TILLEY (M.O.H. for Northumberland) spoke of "the responsibilities of the hospitals outside the hospitals"—where patients spend the greater part of their lives. He thought it part of the hospital's responsibility to make proper use of the local health authority's services when their patients go home.

SUMMING-UP

Lord COHEN, in conclusion, said that responsibility involves personal relationships, and no administrative edict or regulations can impose a cooperative will on those who do not want to cooperate. Given the will to cooperate, there is usually little need for any regulations or administrative structure. General principles of responsibility cannot be enunciated, because the principles differ according to the type of hospital and the type of situation; upon the people concerned; and to some extent also on the geographical situation.

Perhaps there is a case for undertaking the study of good hospital practice and of bad hospital practice:

"Why are some hospitals good? Why is the relationship between the members of the staff and the different departments good? Why, in other places, is it bad? Why, in some hospitals, is the general practitioner allowed to visit whenever he wishes? . . . These are matters which I think might be gone into, and especially in relation to the results of the treatment in various types of hospitals."

From personal experience Lord Cohen suspected that, if everybody who practises in a hospital had a really serious illness treated in that hospital, we should discover where the machinery has gone wrong.

But hospital treatment is really but an incident in the patient's illness, and it is important to realise that the public of today is an educated public, and that the patient has a right to know certain things about himself. He wants to know where he stands in relation to his job, in relation to the future, and in relation to his own family, and the consensus of this symposium seemed to be that this indeed cannot be denied him.

The patient must always be the prime consideration, and two aspects of his welfare had been stressed. The first is the need for ensuring that the surroundings in which he is treated are free from risk. The second is his personal relationship with a doctor. "I doubt if there is a personal relationship, ever, between a team and a patient; the relationship must be a direct one with one member of the team. Sometimes it may not be the general practitioner, though I hope that in most cases it would."

One of the problems which had arisen is how to coordinate departments which too often work in relative isolation.

"I have often thought that a hospital should in its activity resemble a tapestry of clear, if changing, design, rather than a patchwork quilt—and it is clear from what has been said that many hospitals resemble the patchwork quilt.

"I have some experience of joint admission wards and I think that they are extraordinarily valuable. In my early days, whether you had medical treatment for your duodenal ulcer, or surgical treatment, depended entirely on the whim of whoever was the clerk in the outpatient department, who referred the patient either to the medical or to the surgical outpatient department. I cannot believe that that is the best form of medicine. It sometimes happens in other ways today; and that is why I have a strong feeling for the joint admission ward, which should be looked after by the senior physician, the senior surgeon, the senior consultants of the hospital, and in which students in teaching hospitals should be forced to take part of their clinical training."

Nothing he had heard led Lord Cohen away from the position taken by the Committee on General Practice which he chaired in 1953.

The report made it clear that the general practitioner must be the linchpin of all health care, and responsible for the continuing care of the patient. It dealt with relationship of the general practitioner to the hospital: it spoke of wards being open at any time, bringing the clinical assistant into the hospital and making the path from general practice to consultant or specialist practice not an impenetrable barrier but one which can possibly be traversed. It spoke of this question of reports to the practitioner. These are provided in many hospitals. Then why not in all? "Is it wholly the result of lack of secretarial help? Can we really lay our hands on our hearts and say that we, as consultants, have no responsibility for this? I personally would doubt it."

One of the most regrettable features of the present situation is the increasing isolation of the regional and teaching hospitals.

"In the old days, many of us deplored the antagonism, the working in separate compartments, of the voluntary and the municipal hospitals; but are we not reaching a very similar stage in many regions in this country, where communication between regional and teaching hospitals is virtually nil? The original concept of regionalisation was, after all, that the whole of the hospital service of a region should be centred on the teaching hospital, and that its standards and activities should radiate from the teaching hospital throughout the region, not in terms of the hierarchy, but in terms of partners, recognising that they have benefits from mutual cooperation. I recall, before the service, presenting a memorandum suggesting that this could be achieved by an appropriate interchange of staffs between teaching and regional hospitals; and I think that that is still possible, and indeed, one of the few ways in which we shall achieve this concept of regionalisation which is a holism in the the hospital service."

Of course there is need for more staff. There is need for more staff in every single branch of the health service:

"I would remind you that since 1948 the number of consultants has doubled, the number of general practitioners has increased by 25% or so, the number of nurses has increased, and so forth. But our responsibilities have increased, and they increase not simply by the passage of time, but by the increasing complexity of diagnosis and treatment, and patient care. But do let us see this in perspective. This is not simply a problem of health care. There is here a national problem. The teachers are asking for far more teachers; the dentists are asking for far more dentists; the psychiatric social workers and others are asking for far more to discharge their duties."

But there is not an inexhaustible pool of man-power and an inexhaustible purse; and therefore there must be appropriate planning, and utilisation of resources to the best advantage, in the interest of the patient.

In England Now

A Running Commentary by Peripatetic Correspondents

"TOBACCO, neomercazole, potassium perchlorate, or surgery." I ran over the choice of treatments as I complacently puffed a smoke ring over the desk, while the second case in my series vested himself in my consulting-room.

The first case (I would have to "steal" him for my series as he was not treated by me) had merited a letter in another journal because he presented with thyrotoxic myopathy. In a "personal communication" he had told me that he dated all his symptoms from giving up smoking in January. By August thyrotoxicosis had manifested itself, masked only by maintenance of weight due to his devoted wife's feeding numerous bars of N.A.A.F.I. chocolate.

Now here was my second case. He had given up smoking in April, when a friend of his at his office, a heavy smoker, died of cancer of the lung. Instead of the expected increase in weight he presented in December with a 19 lb. loss. His staring eyes faced me across the desk and he admitted to tremor. To my satisfaction I found his thyroid enlarged. I recommended he saw a thyroid surgeon and hastened to report the increase in my series to my senior partner, whose car's no longer found littered with empty packets of "Senior Service". As I retailed the case, giving vent to my theories on the dangers of stopping smoking, our secretary, sitting discreetly in the corner, remarked, "I'd develop thyrotoxicosis married to that patient's wife." Reluctantly I crossed tobacco off my mental therapeutic index, but I still wonder.

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The New Year hit us like a north-easterly gale. It seemed that all the world had nursed their ailments until Monday—the first working day of 1961. Calls came pouring in, and to add to our discomfort one partner went down with epidemic vomiting. We battled on till Saturday morning, when to crown it all one of my booked "midders" started in labour two weeks early. The day looked busy enough without this added complication. She was a para-2 with plenty of room; so I knew it would not be long once the second stage was reached. At 11.30 P.M. her pains had virtually ceased. A large dose of chloral was exhibited. The nurse went to bed in the next room, and I went home expecting to be called in the small hours.

It was about 4 A.M. and I could not understand why I had not been called because the pains were getting stronger and were now continuous. When I did awake it slowly dawned on me that it was I who had the pains. And what was more they had become localised in the right inguinal fossa. A very unhealthy vermiform appendix was delivered at 11.45 A.M. on Sunday morning.

The midder? Oh she was delivered spontaneously with no trouble at all at 11.45 A.M. the following day, by the district nurse.

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My disgruntled "Why?" to the cry "Come at once, Doctor" was answered by our receptionist's doom-laden words, "The lion trainer has collapsed." Her reply promised a domiciliary visit that would for once be exciting as well as urgent.

When I had visited the circus the previous day I had had a premonitory qualm and my rapt children gave a sibilant indrawn breath when Fearless Frank in leopard-skin bikini, leather-thonged from calf to sandal, had popped his head into the lion's mouth. Now I knew the worst had happened. The lion, replete and bored, had yawned at the exact moment when Fearless Frank placed his head in the jaws, and Frank's poll was completely enclosed with his mandible resting on the back of the feline incisors.

I saw myself handing the Mannlicher to a renal dwarf—Ticky, our thimble-size clown—with the exhortation, "Don't shoot unless I signal; remember to aim for the shoulder shot. Fire both barrels." Reluctantly I entered the cage holding a chair to prod in the direction of the big cats who were snarling and pawing the sawdust. Limp Fearless Frank's scalp was still pressed firmly against Big Nell's (or was it Little Tom's) uvula and I shouted "Blow down the beast's throat" to make the latter gag and reject the polished cranium instead of nipping it off like a wart on a stalk. The lion was unlikely to yawn again and unless my plan was effective Fearless Frank was a Daniel come to judgment. The Moment of Truth, the bullets would crush the lion's chest and in reflex the jaws might open—or close.

The receptionist's voice brought reality. "You can't go. The waiting-room is full." I peeped round the door—at least a dozen impatient neurotics—and fantasy departed. "You're quite right, sister. Yes, my duty is with the N.H.S., my wife, and my children. Even if the headlines . . ." She raised her eyebrows in surprise, and recovering quickly I went on, "Yes, Dr. Smith is on call—ask if he would be so kind as to go."

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"Of course, they never tell you anything in hospitals." Well, at one hospital they certainly do. I asked the patient whether she knew what was done at her last operation. "Oh, yes," she said. "The surgeon, himself, told me everything he done—he opened me stomach, removed all me juices, washed me gall bag, and took a fleck from out of me windpipe."

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I hasten to warn applicants for a job as an industrial medical officer not to be misled by the peripatetic advice given to potential company medical advisers. A colleague who was recently short-listed for a post in industrial medicine began by spending a night with six other aspirants in a gloomy northern hotel. Their bedrooms were unheated, but their shivering reflexes enabled them to survive. They were collected early in the morning and, after a tour of the factory, were inspected over coffee by the nursing staff. There was then a prolonged wait in a lavish anteroom before they were ushered into a setting appropriate to a foreign ministers' conference. Alternating round the boardroom table were places for candidates and assessors; in front of each candidate a plaque with his name. The only person with a nervous twitch was the tame psych—an assessor.

First each gave a potted life history—assessors included. The most interesting information was the boxing weight of one of the contestants. Then a topic for discussion was read out, and the assessors withdrew to the corners of the room. My friend would not normally have joined this particular discussion, even if he had understood the subject, but he felt that some contribution was expected (after all they were paying his travelling expenses). However, a "natural leader" had already selected himself, which left my friend free, after a few mumbled words, to listen with awe to the eloquent wisdom of the others. After a time the assessors drew up their chairs and joined in.

The lunch was indeed sumptuous, but the candidates were able to dunk their soup and gnaw the bones unobserved except by minions. The examining panel dined with their peers. In the afternoon there were more orthodox individual interviews. Here my friend was faced with the usual difficulty where examiners are a group of lay and medical men, for while it is easy to talk on medical matters with colleagues (unless they are pathologists conducting a viva), it is not easy to make a reasonable showing before the combination. Professional baby language goes down no better with the doctor than jargon with the layman.

No one was more surprised at the outcome than the successful candidate, and it is doubtful if he could give any tips on deportment. It was rumoured that the actual selection was made by the chauffeur who drove them to the station after the interview.

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A doctor, a long-suffering employee of a regional hospital board, dreamt that he had had an enormous pools win. In his dream he decided to stop working and immediately informed the regional board of his decision. He sent them a telegram couched in the following terms: "B—— you for a start; abusive letter follows."

GENERAL PRACTITIONER, HOSPITAL, AND LOCAL AUTHORITY

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From personal experience Lord Cohen suspected that, if everybody who practises in a hospital had a really serious illness treated in that hospital, we should discover where the machinery has gone wrong.

But hospital treatment is really but an incident in the patient's illness, and it is important to realise that the public of today is an educated public, and that the patient has a right to know certain things about himself. He wants to know where he stands in relation to his job, in relation to the future, and in relation to his own family, and the consensus of this symposium seemed to be that this indeed cannot be denied him.

The patient must always be the prime consideration, and two aspects of his welfare had been stressed. The first is the need for ensuring that the surroundings in which he is treated are free from risk. The second is his personal relationship with a doctor. "I doubt if there is a personal relationship, ever, between a team and a patient; the relationship must be a direct one with one member of the team. Sometimes it may not be the general practitioner, though I hope that in most cases it would."

One of the problems which had arisen is how to coordinate departments which too often work in relative isolation.

"I have often thought that a hospital should in its activity resemble a tapestry of clear, if changing, design, rather than a patchwork quilt—and it is clear from what has been said that many hospitals resemble the patchwork quilt.

"I have some experience of joint admission wards and I think that they are extraordinarily valuable. In my early days, whether you had medical treatment for your duodenal ulcer, or surgical treatment, depended entirely on the whim of whoever was the clerk in the outpatient department, who referred the patient either to the medical or to the surgical outpatient department. I cannot believe that that is the best form of medicine. It sometimes happens in other ways today; and that is why I have a strong feeling for the joint admission ward, which should be looked after by the senior physician, the senior surgeon, the senior consultants of the hospital, and in which students in teaching hospitals should be forced to take part of their clinical training."

Nothing he had heard led Lord Cohen away from the position taken by the Committee on General Practice which he chaired in 1953.

The report made it clear that the general practitioner must be the linchpin of all health care, and responsible for the continuing care of the patient. It dealt with relationship of the general practitioner to the hospital: it spoke of wards being open at any time, bringing the clinical assistant into the hospital and making the path from general practice to consultant or specialist practice not an impenetrable barrier but one which can possibly be traversed. It spoke of this question of reports to the practitioner. These are provided in many hospitals. Then why not in all? "Is it wholly the result of lack of secretarial help? Can we really lay our hands on our hearts and say that we, as consultants, have no responsibility for this? I personally would doubt it."

One of the most regrettable features of the present situation is the increasing isolation of the regional and teaching hospitals.

"In the old days, many of us deplored the antagonism, the working in separate compartments, of the voluntary and the municipal hospitals; but are we not reaching a very similar stage in many regions in this country, where communication between regional and teaching hospitals is virtually nil? The original concept of regionalisation was, after all, that the whole of the hospital service of a region should be centred on the teaching hospital, and that its standards and activities should radiate from the teaching hospital throughout the region, not in terms of the hierarchy, but in terms of partners, recognising that they have benefits from mutual cooperation. I recall, before the service, presenting a memorandum suggesting that this could be achieved by an appropriate interchange of staffs between teaching and regional hospitals; and I think that that is still possible, and indeed, one of the few ways in which we shall achieve this concept of regionalisation which is a holism in the the hospital service."

Of course there is need for more staff. There is need for more staff in every single branch of the health service:

"I would remind you that since 1948 the number of consultants has doubled, the number of general practitioners has increased by 25% or so, the number of nurses has increased, and so forth. But our responsibilities have increased, and they increase not simply by the passage of time, but by the increasing complexity of diagnosis and treatment, and patient care. But do let us see this in perspective. This is not simply a problem of health care. There is here a national problem. The teachers are asking for far more teachers; the dentists are asking for far more dentists; the psychiatric social workers and others are asking for far more to discharge their duties."

But there is not an inexhaustible pool of man-power and an inexhaustible purse; and therefore there must be appropriate planning, and utilisation of resources to the best advantage, in the interest of the patient.

In England Now

A Running Commentary by Peripatetic Correspondents

"TOBACCO, neomercazole, potassium perchlorate, or surgery." I ran over the choice of treatments as I complacently puffed a smoke ring over the desk, while the second case in my series vested himself in my consulting-room.

The first case (I would have to "steal" him for my series as he was not treated by me) had merited a letter in another journal because he presented with thyrotoxic myopathy. In a "personal communication" he had told me that he dated all his symptoms from giving up smoking in January. By August thyrotoxicosis had manifested itself, masked only by maintenance of weight due to his devoted wife's feeding numerous bars of N.A.A.F.I. chocolate.

Now here was my second case. He had given up smoking in April, when a friend of his at his office, a heavy smoker, died of cancer of the lung. Instead of the expected increase in weight he presented in December with a 19 lb. loss. His staring eyes faced me across the desk and he admitted to tremor. To my satisfaction I found his thyroid enlarged. I recommended he saw a thyroid surgeon and hastened to report the increase in my series to my senior partner, whose car's no longer found littered with empty packets of "Senior Service". As I retailed the case, giving vent to my theories on the dangers of stopping smoking, our secretary, sitting discreetly in the corner, remarked, "I'd develop thyrotoxicosis married to that patient's wife." Reluctantly I crossed tobacco off my mental therapeutic index, but I still wonder.

* * *

The New Year hit us like a north-easterly gale. It seemed that all the world had nursed their ailments until Monday—the first working day of 1961. Calls came pouring in, and to add to our discomfort one partner went down with epidemic vomiting. We battled on till Saturday morning, when to crown it all one of my booked "midders" started in labour two weeks early. The day looked busy enough without this added complication. She was a para-2 with plenty of room; so I knew it would not be long once the second stage was reached. At 11.30 P.M. her pains had virtually ceased. A large dose of chloral was exhibited. The nurse went to bed in the next room, and I went home expecting to be called in the small hours.

It was about 4 A.M. and I could not understand why I had not been called because the pains were getting stronger and were now continuous. When I did awake it slowly dawned on me that it was I who had the pains. And what was more they had become localised in the right inguinal fossa. A very unhealthy vermiform appendix was delivered at 11.45 A.M. on Sunday morning.

The midder? Oh she was delivered spontaneously with no trouble at all at 11.45 A.M. the following day, by the district nurse.

* * *

My disgruntled "Why?" to the cry "Come at once, Doctor" was answered by our receptionist's doom-laden words, "The lion trainer has collapsed." Her reply promised a domiciliary visit that would for once be exciting as well as urgent.

When I had visited the circus the previous day I had had a premonitory qualm and my rapt children gave a sibilant indrawn breath when Fearless Frank in leopard-skin bikini, leather-thonged from calf to sandal, had popped his head into the lion's mouth. Now I knew the worst had happened. The lion, replete and bored, had yawned at the exact moment when Fearless Frank placed his head in the jaws, and Frank's poll was completely enclosed with his mandible resting on the back of the feline incisors.

I saw myself handing the Mannlicher to a renal dwarf—Ticky, our thimble-size clown—with the exhortation, "Don't shoot unless I signal; remember to aim for the shoulder shot. Fire both barrels." Reluctantly I entered the cage holding a chair to prod in the direction of the big cats who were snarling and pawing the sawdust. Limp Fearless Frank's scalp was still pressed firmly against Big Nell's (or was it Little Tom's) uvula and I shouted "Blow down the beast's throat" to make the latter gag and reject the polished cranium instead of nipping it off like a wart on a stalk. The lion was unlikely to yawn again and unless my plan was effective Fearless Frank was a Daniel come to judgment. The Moment of Truth, the bullets would crush the lion's chest and in reflex the jaws might open—or close.

The receptionist's voice brought reality. "You can't go. The waiting-room is full." I peeped round the door—at least a dozen impatient neurotics—and fantasy departed. "You're quite right, sister. Yes, my duty is with the N.H.S., my wife, and my children. Even if the headlines . . ." She raised her eyebrows in surprise, and recovering quickly I went on, "Yes, Dr. Smith is on call—ask if he would be so kind as to go."

* * *

"Of course, they never tell you anything in hospitals." Well, at one hospital they certainly do. I asked the patient whether she knew what was done at her last operation. "Oh, yes," she said. "The surgeon, himself, told me everything he done—he opened me stomach, removed all me juices, washed me gall bag, and took a fleck from out of me windpipe."

* * *

I hasten to warn applicants for a job as an industrial medical officer not to be misled by the peripatetic advice given to potential company medical advisers. A colleague who was recently short-listed for a post in industrial medicine began by spending a night with six other aspirants in a gloomy northern hotel. Their bedrooms were unheated, but their shivering reflexes enabled them to survive. They were collected early in the morning and, after a tour of the factory, were inspected over coffee by the nursing staff. There was then a prolonged wait in a lavish anteroom before they were ushered into a setting appropriate to a foreign ministers' conference. Alternating round the boardroom table were places for candidates and assessors; in front of each candidate a plaque with his name. The only person with a nervous twitch was the tame psych—an assessor.

First each gave a potted life history—assessors included. The most interesting information was the boxing weight of one of the contestants. Then a topic for discussion was read out, and the assessors withdrew to the corners of the room. My friend would not normally have joined this particular discussion, even if he had understood the subject, but he felt that some contribution was expected (after all they were paying his travelling expenses). However, a "natural leader" had already selected himself, which left my friend free, after a few mumbled words, to listen with awe to the eloquent wisdom of the others. After a time the assessors drew up their chairs and joined in.

The lunch was indeed sumptuous, but the candidates were able to dunk their soup and gnaw the bones unobserved except by minions. The examining panel dined with their peers. In the afternoon there were more orthodox individual interviews. Here my friend was faced with the usual difficulty where examiners are a group of lay and medical men, for while it is easy to talk on medical matters with colleagues (unless they are pathologists conducting a viva), it is not easy to make a reasonable showing before the combination. Professional baby language goes down no better with the doctor than jargon with the layman.

No one was more surprised at the outcome than the successful candidate, and it is doubtful if he could give any tips on deportment. It was rumoured that the actual selection was made by the chauffeur who drove them to the station after the interview.

* * *

A doctor, a long-suffering employee of a regional hospital board, dreamt that he had had an enormous pools win. In his dream he decided to stop working and immediately informed the regional board of his decision. He sent them a telegram couched in the following terms: "B—— you for a start; abusive letter follows."

Letters to the Editor

BRETYLIUM AND GUANETHIDINE

SIR,—Reading through your leading article (Jan. 14) one is left with the impression that bretylium and guanethidine in therapeutic doses possess only one pharmacological action: the blocking of adrenergic neurones. Unfortunately, this is not the case.

From animal experients [1 2] it is quite clear that these substances produce changes in nearly all effector cells innervated by either cholinergic or adrenergic neurones. One of the most obvious changes is an increased sensitivity of the blood-vessels to noradrenaline, adrenaline, and any other substance stimulating or inhibiting smooth-muscle activity. This sensitisation, sometimes very marked, is independent of the blockade of the adrenergic neurones. A similar sensitisation to noradrenaline and adrenaline has been found in man (D. R. Laurence, personal communication).

Thus, two antagonistic effects may appear simultaneously: a blockade of adrenergic neurones tending to reduce the vasoconstrictor tone, and a direct effect on the blood-vessels tending to make them more sensitive to any vasoconstrictor or vasodilator substance. Because of this, the final effect on the arterial blood-pressure will depend on whether it is the adrenergic-blocking activity or the direct peripheral effect which predominates. In cases where the balance between the adrenergic-blocking and the sensitising properties is weighted in favour of the former, the patient will benefit from the use of these drugs; in contrast, when the sensitising tendency is the dominant one, or the intrinsic vascular activity is high, the therapeutic results will be poor and any increase in the dose administered will intensify the side-effects without further reducing the arterial blood-pressure.

From clinical reports, especially on bretylium, it appears that very often the doses used in hypertensive patients are far above those needed to produce a blockade of adrenergic neurones. The reason advanced for giving large doses is that some patients are " insensitive " to the drugs from the beginning, or that they quickly develop " tolerance ". A marked development of true tolerance, however, is not in accordance with the results obtained in animal experiments, where, no matter what adrenergic pathway is tested, no such phenomenon occurs. I should like, therefore, to put forward the suggestion that " insensitivity " of the patients to bretylium and guanethidine appears, not because the drugs fail to block adrenergic transmission, but because this is masked by the simultaneous peripheral sensitisation of the blood-vessels to noradrenaline and adrenaline. The therapeutic doses, therefore, should be kept as low as possible—that is, to the minimum needed to block adrenergic transmission—and my conviction is that the clinicians will find this dose varying little from patient to patient. Tests estimating adrenergic activity (the Valsalva manœuvre, &c.) should be carried out in order to determine the appropriate dose for every patient. Once the adrenergic neurones are blocked, a further increase in the dose will only produce more undesirable changes in the various effector cells. I fail to see that there can be any instance in which an increase in the administered dose, above that which blocks adrenergic transmission, could be of any use to the patient. On the other hand, I can think of many unwanted effects which might appear when large doses are used.

Department of Pharmacology,
Royal Free Hospital School of Medicine,
London, W.C.1. ELEANOR ZAIMIS.

1. Zaimis, E. *Nature, Lond.* 1960, **187**, 213.
2. Vernikos-Danellis, J., Zaimis, E. *Lancet*, 1960, ii, 787.

SIR,—I agree with most of the observations in your leading article. You may, however, allow me a few comments on points of dissent.

While the development of tolerance to bretylium is a drawback, it is by no means universal and I still have over 20 patients who have been satisfactorily controlled with this drug for a period exceeding a year. Tolerance occurs also, although less commonly, with guanethidine; this has been reported by others and observed by me. Guanethidine has not only a more constant inhibitory effect on ejaculation than bretylium but, contrary to your statement, not infrequently affects libido. Guanethidine also may cause exertional hypotension although less commonly than bretylium. The observation that in healthy subjects small oral doses of guanethidine are not associated with any change in inulin clearance or electrolyte excretion has been confirmed by Bonomini.[1] He found that, while large intravenous doses of bretylium and guanethidine depressed renal function in patients with hypertension due to chronic pyelonephritis, slow infusion of smaller doses did not materially affect renal plasma-flow.

I would like to confirm Leishman's advice [2] to increase the dose of guanethidine much more cautiously than the Hammersmith workers. If 30 mg. is given as a starting dose with increases by 30 mg. every third day as advised by Dollery et al.[3] untoward effects will be inevitable in some cases. Overdosage is more dangerous with guanethidine than with bretylium because of the longer-continued effect of guanethidine.

Finally I would like to call attention to the danger of cardiac arrest under anæsthesia in patients receiving either of these drugs. At the Whittington Hospital we have had such a case in a patient who survived with prompt resuscitation, and I know of at least one other case at another hospital. Vernikos and Zaimis [4] showed that vagal reflexes are greatly enhanced by either bretylium or guanethidine. The anæsthetic department at Whittington has made it a practice to give larger doses of atropine than usual as premedication, and it would seem wise for this practice to be adopted generally.

Whittington Hospital,
London, N.19. E. MONTUSCHI.

1. Bonomini, V. Communication to Symposium on Hypertension, Milan, 1960.
2. Leishman, A. W. D., Matthews, H. L., Smith, A. J. *Lancet*, 1959, ii, 1044.
3. Dollery, C. T., Emslie-Smith, D., Milne, M. B. *ibid.* 1960, ii, 381.
4. Vernikos, J., Zaima, E. J. *ibid.* p. 787.

PER ARDUA AD ARDUA

SIR,—The cell biologists may answer for themselves; but at least Dr. McClure [5] has given expression in a masterly manner to the frustrations of all those who read extensively the literature of research, and who chafe at the apparent lack of connection between the swiftly growing ramifications—or perhaps of the multiplication of dead ends—of the various technologies. But I submit that the conclusions which Dr. McClure draws from his study of the activities of the cell biologists in particular are quite misguided.

His most important conclusion is that much research in cell biology is futile or aimless, that the processes of the cell are beyond human understanding, and hence by implication that research into ageing is equally futile, and even undesirable, and philosophy should take its place. The author speaks of a philosophy of life, but here he really means a philosophy of death or resignation.

All this has a somewhat familiar ring, and if these opinions had been expressed from the pulpit rather than in *The Lancet*, doubtless they would have been received by a congregation with awed respect.

It is true that research has not yet revealed what actuates the parts and processes of the living cell; but it is demonstrably possible to manipulate matter, which includes living matter, without knowing what it is or how it works, and to alter its behaviour without knowing clearly how one does it. And while

5. McClure, D. M. *Lancet*, 1960, ii, 1388.

it may be equally true that the " perpetual continuity of function of any living organism " cannot be ensured, the extension of the span of life of some organisms can be achieved by the simplest of manipulations.

Take for example the cabbage. The span of life of this edible biennial can be greatly prolonged when seeding is prevented by control of the environmental temperature.[6 7] By cutting off the flower primordia of *Reseda odorata* the life of this annual can be extended by several years,[8] although it is quite unknown why in monocarpic plants the maturing of fruits leads to death. Numerous other examples of the extension of the life of plants can be cited.

More spectacular is the work of Williams [9] and Wigglesworth [10] on the juvenile hormone in insects, where application to the insect of material containing this hormone caused the adult cuticle of *Rhodnius* and *Tenebrio* to revert to larval cuticle. This is, although the analogy is not quite exact, as though application of some substance to the bearded adult chin caused the skin to revert to the juvenile beardless condition.

In the case of mammals, where the built-in homœostatic mechanisms are more elaborate, manipulations of the internal milieu are notoriously difficult; but it is only necessary to mention McCay's [11 12] successful extension of the life of the laboratory rat to about twice the maximum age reached by normal controls to show that research into the biology of ageing has not been lacking in achievement.

The number of laboratory workers in this field is limited, perhaps for the reason that aged humans rarely, if ever, die from the deteriorations consequent on ageing, but rather from the attendant pathological processes the study of which is more immediately rewarding; perhaps also because among laymen and many medical men, as opposed to zoologists, there is still a feeling that such work is not only futile but lacks status.

Surely the correct way to regard gerontological research is that it is an important, although embryonic, part of preventive medicine?

The long survival of McCay's rats was accompanied by a decreased incidence of chronic disease, particularly pulmonary diseases and tumours. Moreover the retarded rat remains active and appears young and alert whatever its chronological age.[12] It is to be noted that this was not a prolongation of the period of senile decrepitude. McCay succeeded in doing in the laboratory what a currently advertised dog-food is said to do.

If it is accepted to be desirable to prolong active life in dogs, it ought to be meritorious to accomplish the same thing in humans, or at least in some humans, which should include Dr. McClure and the present writer.

It may well be therefore that time and funds devoted to basic research in ageing might entrain much sooner a greater relief of suffering than the present piecemeal attack on the individual diseases which beset old people.

Lastly I suggest that the next important advance in the biology of ageing will most probably be made at a time when the cytologists are still struggling to elucidate the dynamics of the microsomes, the mitochondria, and the cytoplasmic membranes.

London, N.W.1. JOHN BRAY.

6. Miller, J. C. *Bull. Cornell agric. Exp. Sta.* 1929, **488**, 46.
7. Curtis, O. F., Clark, D. G. Introduction to Plant Physiology; p. 623. London, 1950.
8. Molisch, H. The Longevity of Plants; p. 128. New York, 1938.
9. Williams, C. M. *Nature, Lond.* 1956, **178**, 212.
10. Wigglesworth, V. B. *J. Insect Physiol.* 1958, **2**, 73.
11. McCay, C. M. *in* Cowdry's Problems of Ageing (edited by A. I. Lansing). Baltimore, 1952.
12. Comfort, A. Biology of Senescence; p. 448. London, 1956.

THE NATURE OF ESSENTIAL HYPERTENSION

SIR,—Correspondence under this title, if not conclusive, has at least been informative. Perhaps, like your Socratic dialogues, it too might be reprinted. Being diffident, but Irish by name, I am reminded of the Irishman who, before entering into what seemed to be an altercation, considerately inquired whether it was a private affair or open to anyone. The letters of Oct. 5 prompt me to make a similar inquiry.

In particular, they raise the question of technique. This can be very important. How important—in another connection—is indicated by Harry Golden's suggestion that integration would be easy in the Southern States if it were vertical, as by removing seats from buses, eating places, theatres and the like. The fact is that taking a blood-pressure may have ominous overtones; it may place in jeopardy the patient's ability to do his job, provide for his family, or see his friends. The greater the apparent professional rank of the observer relative to that of the patient, the greater the anxiety. Hence, perhaps the most representative pressures would be those taken by the patients themselves. The next best approximation would be a pressure taken by a technician whose manner and speech correspond roughly to those of the patient.

While I believe these opinions can be supported, it seems to me that the problem of technique has been well reviewed at the Princeton Conference on Methodology in Epidemiology of Cardiovascular Diseases.[1] The recommendations from this group may not reveal the nature of essential hypertension instantly and to everyone's satisfaction; but they may diminish the areas of controversy.

Department of Clinical Investigation,
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Cleveland, Ohio. A. C. CORCORAN.

ESSENTIAL-FATTY-ACID CONTENT OF HENS' EGGS

SIR,—Dr. Coppock and his colleagues (Jan. 14) have reported nothing that causes me to withdraw the statement I made in the television interview to which they refer. This was as follows: " There are good and bad chickens. I am in favour of the backyard hen, but I am not so certain about the broiler and the battery-fed hen." I said the same remarks applied to eggs of battery hens and farmyard hens. It has been known for more than twenty years that the E.F.A. content of the egg depends on that of the diet of the hen. The powerful combination of Spillers and B.O.C.M. (Unilever) has shown that battery and free-range birds eating roughly the same amounts of E.F.A. (1·24% and 1·52%) have roughly the same amounts of E.F.A. in their eggs (15·3% and 16·1%). This is what one would expect. The free-range hens I worked with ate (amongst other things) seeds (high in linoleic acid), greenstuff (60% of the fat of which may be linolenic acid), insects (some of which contain fat of which 60% is linoleic acid), and earthworms (the phospholipids of which are very rich in arachidonic acid). How, I wonder, did Dr. Coppock collect for analysis the natural diet of the farmyard hen?

My preference, on present evidence, for eggs from farmyard rather than battery hens was based on a simple experiment I did in the summer of 1956. I allowed the eggs of each type to be fertilised, hatched the chicks, and found material staining red with Sudan IV in the aortas of the day-old chicks from eggs of battery hens and not in those of free-ranging hens. Some of the chicks of the former type were then reared indoors on a commercial meal, and in these when killed the fatty deposits were greater whereas there were none in the chicks of the same origin reared free-ranging. I should like to follow up this work, given (I hope by your correspondents) a battery, some meal, and a gas-liquid chromatograph, because eggs are a very important item of our dietaries and have come under suspicion, perhaps wrongly, because of their efficiency in raising serum-cholesterol.

Oxford. HUGH SINCLAIR.

1. See *Amer. J. publ. Hlth*, Oct. 1960.

PULMONARY HYPERTENSION

SIR,—Dr. Goodwin [1] has listed all the described signs of right ventricular enlargement and with this list nobody will disagree. But he misses the crux of the discussion—namely, an ability to detect *all* these signs when the right ventricular enlargement is only *slight*, as it was in his case.[2]

Dr. Fletcher [3] irrelevantly imputes to me very peculiar views about the M.R.C.P. examination. I am willing to accept his criterion of auscultatory ability—that is, comparison of the clinician's findings with a previously unseen phonocardiogram (provided that there is agreement concerning the interpretation of the latter). Such a test on a series of selected patients could be easily arranged and I would be willing to cooperate with the arrangements, provided that the clinicians taking part agreed to detailed publication of the results. Dr. Fletcher mentions that Dr. Goodwin is an F.R.C.P. and, being also a Fellow, he might welcome an opportunity to demonstrate his powers.

Since reading Dr. Fletcher's letter, I have tested out many people and find that the great majority cannot in fact count 5 ticks per second. But even this is perhaps irrelevant because the 5 ticks are of equal intensity and equally spaced, and there is no attempt to recognise each of the 5 separately and individually as is done with heart-sounds. The main purpose of my letter was to arouse an honest discussion on the whole subject of heart-sounds.

London, W.1. M. H. PAPPWORTH.

INFECTION FROM POULTRY

SIR,—In your annotation of Jan. 7 you say: "If the bird is not cooked thoroughly someone is going to get the merry-go-whimbles."

I would point out that only one instance of transmission of *Salmonella typhimurium* (or for that matter any other salmonella infection) from poultry to man in this country has been recorded.[4] Infection was transmitted to 3 poultry-keepers who attempted a "home necropsy" on some dead turkey poults aged about 7 days.

In nearly forty years with the poultry industry I have seen thousands of chicks and poults die of salmonellosis and have investigated cases from Cornwall to the Orkneys. Hundreds of poultry-keepers and their assistants have handled infected carcasses and attended to sickly stock; I have not heard of a single case of infection being transmitted to man other than the one recorded.

The organisms implicated and isolated from infections I have attended have been *S. pullorum* (anaerogenic and aerogenic), *gallinarum*, *typhimurium*, *bareilly*, *meleagridis*, *thompson*, *newport*, *stanleyville*, and *enteritidis*. The most severe and damaging mortality in the poultry under review has arisen from the anaerogenic types—*pullorum* and *gallinarum*. On a par with this observation, one could specify *S. typhi*, also an anaerogenic organism, as the really dangerous type for man. In the recorded case the *typhimurium* was an anaerogenic type.

The veterinary profession is concerned with the possible emergence of antibiotic-resistant strains because of the use of antibiotics in feeding-stuffs and in slush-ice in processing. Is more significance to be attached to the emergence of antibiotic-resistant strains than to phenol-resistant strains of *Escherichia coli* or other potential pathogens? Must one refuse to make vaccines because an organism remains viable after 48 hours' suspension in 0·5% phenol?

It seems to me fallacious to reason by analogy from raw eggs to cooked carcasses. Once when I investigated the rot of eggs during incubation I was surprised to culture *S. pullorum* in pure culture from a black-rot egg submitted. The laying flock, which was accredited, had had previous blood-tests and had been declared free of pullorum infection; subsequent testing failed to discover the offending layer. In rearing many thousands of poults from the flock all attempts to isolate this organism from any dead or sickly poults were negative.

But I have good evidence that the washing of eggs or even permitting rain to wet eggs during collection or handling is the most potent source of fæcal invasion of the egg contents. A wet membrane apparently no longer acts as a barrier to potential pathogens. At one time poult mortality from fæcal invasion—proteus, coliforms, enterococci, staphylococci—became such a toll that we had to discontinue the washing of eggs, even in officially recommended antiseptics. We installed buffing machines at all our farms to dry-clean contaminated eggs. Since that time rot of eggs and poult mortality from this cause have ceased.

Hence it is apparent that, while eggs may be quite dangerous under man-made hygienic conditions, there is very little evidence that carcasses are dangerous.

W. A. Motley, Ltd.,
Andover,
Hants.

T. BARTON MANN
Director of Veterinary Research.

1. *Lancet*, 1960, ii, 1349.
2. *ibid.* p. 781.
3. *ibid.* p. 1451.
4. Pereira, M. S., Blaxland, J. D. *Mon. Bull. Minist. Hlth Lab. Serv.* 1955, **14**, 52.

PROGNOSIS AND ANTICOAGULANT PROPHYLAXIS AFTER CORONARY OCCLUSION

SIR,—The paper of McMichael and Parry [1] and your leading article on myocardial infarction [2] have rightly brought out the fact that once anticoagulant therapy has been started it is difficult to know when it is wise or safe to discontinue this regimen. The problem does not depend on the particular thromboembolic condition for which therapy was started. Unfortunately some physicians appear to have interpreted the two items in your columns as a criticism of the general use of anticoagulants. Such an inference is unfair to Professor McMichael, who has publicly stated that he favours their use in properly selected cases of thrombophlebitis, pulmonary embolism, multiple embolism from fibrillating hearts, and in the first three months after myocardial infarction.[3] This is a considerable advance on the view of a small but vocal group of clinicians with limited experience of these drugs or none at all, who have denounced them as poisonous and too dangerous (both criticisms apply to many useful drugs used improperly).

The immediate question raised by McMichael and Parry [1] is whether the continuous use of anticoagulants is justified after the first three months in patients who have had myocardial infarction, and, if so, for how long. The authors present no new data, but reassess the figures of others. These data are reviewed critically and in detail, but it seems that the authors are eager to establish some arbitrary cut-off date for discontinuing treatment. This is probably as unsound as the stand that all anticoagulant therapy should be continued for life. But a short period must appeal to certain groups concerned, the social planners who foresee budgetary and organisational difficulties if 1% of the population receives long-term anticoagulant therapy, those physicians who are unsure of the technique, due either to lack of training or of facilities, or are unwilling to carry out the detailed observation required, and patients inconvenienced or bored by tests and constant supervision by their doctors. These and other factors all determine the number of patients who actually continue treatment; but its *scientific value* should not be decided on the basis of a popularity contest. This decision should rest, instead, on the facts and conclusions reached by those who have had large experience with these drugs, and especially by those who have analysed their series with simultaneous controls, preferably selected on a random-sampling or carefully matched basis. All the large series do not meet these criteria fully, as McMichael and Parry pointed out; but it is noteworthy that almost all these

1. McMichael, J., Parry, E. H. O. *Lancet*, 1960, ii, 991.
2. *ibid.* p. 1233.
3. McMichael, J. Discussion at Seraphimer Hospital, Stockholm, Dec. 5, 1960.

workers concluded that this therapy is valuable.[4–14] Criticism has come mainly from those with limited experience or none at all.

McMichael and Parry object to the comparison of data from series in which the treated and control groups were not from the same population-groups, being either from different periods or from different geographical areas. Our own studies published during the past twenty years are in complete agreement. However, these authors themselves then use such comparisons of totally unmatched and miscellaneous series representing different age-groups, periods, and areas to establish their premises. We think that if such comparisons are undesirable to prove a point they are equally undesirable when used to disprove it. It is certainly desirable to subgroup patients of comparable age, sex, weight, blood-pressure, cholesterol levels, &c.; but when this is done some subgroups of even the largest available series are too small to allow valid conclusions to be drawn. Investigators have had at times to use larger groups, and subgroups of sufficient size to give figures of value; any additional conclusions must be by inference, and hence tentative and based on the best evidence to date.

McMichael and Parry are correct in stating that conclusions from small series cannot be definitive. Yet, though they challenge some of the conclusions of the larger Bjerkelund series [12] and the Medical Research Council report,[13] they accept without question the study of Marshall and Shaw,[14] as follows: "Antiprothrombin drugs have also failed in cerebrovascular occlusive disease." They studied a total of 26 treated cases and 25 control cases. In these disease states statistical manipulation cannot produce definitive conclusions from such a small group. Furthermore these results differ from those of larger series reported by Millikan et al.[15] and Carter.[16] The experience of our own group,[17] with 183 cases of stroke which were fully followed up—selected by a strict random-sampling method—corresponds with that of Carter. The relatively small number of women studied to date have failed to produce valid statistics either for or against the long-term value of this treatment.

While, as McMichael and Parry state, there is evidence that coronary thrombosis may occur during anticoagulant therapy, the difference in Bjerkelund's series of 58% in the untreated group and 28% in the treated group is impressive. The series of Capeci and Levy [18] consisted of 100 patients who had had a myocardial infarction and on whom necropsy had been performed in the years 1946–1953. They were not a clinical series selected by random sampling, nor were they part of a study-group specially observed during life. Since only necropsy cases were included, this study gave no information on the survival or clinical complication rates in the treated as against the control group. In most hospitals in the New York area, during that period, anticoagulants were administered largely to those patients who appeared most seriously ill—especially those with definite clinical evidence of thromboembolic complications. There is no evidence that this series was not so biased—which would result in a larger proportion of treated cases showing thromboembolic complications, whereas the control series would tend to be weighted by a relatively larger proportion of deaths from other causes such as non-thrombotic occlusion, cardiac failure, and arrhythmia.

The carefully documented study, involving 1031 patients, of the use of anticoagulants during the acute phase of the first month, reported by the American Heart Association Committee [19] reported in detail very striking differences in the thromboembolic complications found at necropsy. Mural thrombi were found in 32% of the treated cases coming to necropsy, but in 63% of the untreated cases. Twice as many chambers or appendages in untreated cases showed thrombi. 125 extracardiac thromboembolic complications were found per 100 untreated cases as against 45 per 100 in treated cases. Even in this planned study where patients were under detailed observation throughout their illnesses, the clinical diagnoses consistently understated the thromboembolic complications found at necropsy; this discrepancy is greater in untreated cases for reasons detailed in the report. These findings demonstrated a decrease in intracardiac and intra-arterial thromboses, as well as venous thrombosis, and pulmonary embolism, although the latter do play an important role.

McMichael and Parry stated that "no reported series shows that anticoagulant treatment in any way affects the pattern of an increasing mortality with age, or benefits older patients. This is thoroughly borne out by Bjerkelund's (1957) results with his older (over 60) patients, whom treatment did not benefit". The actual figures in Bjerkelund's series were as follows (p. 145): "In the treated group over 60, of 58 patients 16 died (27%); in the untreated group of 55 patients 23 died (42%)." These figures may not be at the 5% confidence level, but they should not be ignored. The Medical Research Council report showed a similar trend in patients over 65 in deaths, severe infarcts, and cardiac failure. The effect of anticoagulant treatment in acute myocardial infarction by age-group in the American Heart Association study is worthy of comment. The death-rates were as follows:

	Total cases		*All cases dying*	
Age-group	*Control*	*Treated*	*Control*	*Treated*
40–49	72	94	11·5%	8·5%
50–59	152	218	12·1%	11·0%
60–69	133	172	32·4%	19·8%
70–79	70	72	42·1%	26·4%

While a confidence level of 5% or lower is desirable at all times and essential in many single studies, attention should be paid to trends which do not quite reach that level, but which are reported again and again. Ignoring such trends, or regarding them as insignificant, may cause us to miss important clues and also the indications for treatment on the basis of the most up-to-date information.

The problem of when to end anticoagulant therapy remains perplexing. I have recently reviewed this subject.[20] Carter and McDevitt [21] in our laboratory described the increase in occlusive and thromboembolic complications observed within the first month or two after stopping long-term therapy. This has been confirmed by Owren,[22] Sise,[23] Dinon and Vander Veer [24] and others. Bjerkelund, however, has told me that he observed no increase; there is no satisfactory explanation of why he differs from the others. These complications were first thought to be due to a "rebound" phenomenon in the clotting mechanism, but neither in our laboratory nor elsewhere has it been possible to establish such a change in the clotting factors. A "rebound" phenomenon would be unlikely to exert its influence for three months or more. It seems more probable that the complications are due to a "catching-up" phenomenon, as additional arterial lumina continue to narrow due to progressive atherosclerosis. They have reached the critical point at which thrombosis would normally occur, but anticoagulants prevent it. The withdrawal of the protective action of anticoagulant therapy allows new thrombi to develop at vulnerable sites. This fits in with the observation that with time results in all treated series become weighted or biased against themselves by the inhibition of the clotting process,

4. Nichol, E. S., Keyes, J. W., Borg, J. F., Coogan, T. J., Boehrer, J. J., Mullins, W. L., Scott, T., Page, R., Griffith, G. C., Massie, E. *Amer. Heart J.* 1958, **55**, 142.
5. Keyes, J. W., Drake, E. H., Smith, F. J. *Circulation*, 1956, **14**, 25.
6. Tulloch, J., Wright, I. S. *ibid.* 1954, **9**, 823.
7. Askey, J. M. Systemic Arterial Circulation. New York, 1957.
8. Suzman, M. M., Ruskin, H. D., Goldberg, B. *Circulation*, 1955, **12**, 338.
9. Owren, P. A. *Northw. Med., Seattle*, 1957, **56**, 298.
10. Manchester, B. *Arch. intern. Med.* 1957, **100**, 959.
11. Friedberg, C. K. *N.Y. St. J. Med.* 1958, **58**, 877, 1303.
12. Bjerkelund, C. J. *Acta med. scand.* 1957, **158**, suppl. 330.
13. *Brit. med. J.* 1959, i, 803.
14. Marshall, J., Shaw, D. A. *Lancet*, 1960, i, 995.
15. Millikan, C. H., Siekert, R. G., Whisnant, J. P. *J. Amer. med. Ass.* 1958, **166**, 587.
16. Carter, A. B. *Lancet*, 1960, i, 345.
17. Wright, I. S. Lecture to the Swedish Medical Society at the 150th Anniversary of the Karolinska Institute, Dec. 6, 1960. To be published.
18. Capeci, N. E., Levy, R. L. *Amer. J. Med.* 1959, **26**, 76.
19. Wright, I. S., Marple, C. D., Beck, D. F. Myocardial Infarction: Report of Committee on Anticoagulants of the American Heart Association; pp. 392–455. New York. 1954. See *Lancet*, 1954, i, 92, 376.
20. Wright, I. S. *Circulation*, 1960, **22**, 608.
21. Carter, S. A., McDevitt, E., Gatje, B. W., Wright, I. S. *Amer. J. Med.* 1958, **25**, 43.
22. Owren, P. A. Personal communication.
23. Sise, H. S., Gauthier, J., Becker, R. *Circulation*, 1959, **20**, 771.
24. Dinon, L. R., Vander Veer, J. B. *Amer. Heart J.* 1960, **60**, 6.

thus prolonging life or postponing complications. But this cannot go on indefinitely if the atherosclerosis progresses. This accounts for the gradual reduction of the favourable differential noted in the first year or two of treatment, especially in series to which new cases are not added. The gains of therapy may thus be rather rapidly lost by stopping anticoagulant therapy and this factor must be reckoned with when considering withdrawal of anticoagulants. When patients have a definite clotting tendency, as in polycythæmia, the situation is still more complex. Almost every week I see such a complication. It makes me hesitate to stop, yet there are many compelling reasons for doing so. All of them must be carefully weighed.

General or categorical recommendations on the duration or the withdrawal of this therapy in patients with thromboembolic disease—whether peripheral, cerebral, or cardiac—seem most inadvisable. Those patients in whom these conditions tend to recur should—other considerations being favourable—have the advantage of continued therapy. Those with a single episode may be on anticoagulants for from one to six months. The decision should then be made by the clinician on the basis of all aspects of the case, including evidence of need, tendency to hæmorrhage, contemplated surgery, ease of control, and practical considerations such as availability of adequate medical and laboratory facilities, time off from work, financial factors, and the wishes of the patient. No decision is irrevocable and subsequent events may necessitate reassessment. Explaining to patients that some risk is involved in stopping the drug will enable them to share the responsibility. It is generally considered sound to withdraw these drugs gradually, but there is no positive evidence that this offers greater protection for the patient. If treatment can be easily carried out and the case is suitable, those with most experience appear to favour continuing anticoagulants after one myocardial infarct, and especially after a second. But clearly conclusive data are still needed.

As McMichael and Parry point out, " recurrent thrombosis may be responsible for a little more than half the ultimate death-rate in patients who have recovered from a cardiac infarction ". Since cardiac infarction involves more than 1,000,000 new patients every year in the western world alone, every effort should be made to delay both these deaths and the thromboembolic complications which may precede and, sometimes, be considered even worse than death itself. Most of these patients will willingly settle for a few more years of life, especially if these can be productive and even if they are only relatively comfortable.

The New York Hospital, New York. IRVING S. WRIGHT.

SIR,—Dr. Triger (Jan. 21) says the routine of anticoagulant therapy after coronary occlusion tends to produce a cardiac neurosis. Doubtless he is correct, but I contend this neurosis is iatrogenic, the doctor being the principal factor in its production.

Few doctors can resist the temptation to display their learning, satisfy their patients' desire to dramatise their ailments, and give respectability to their mode of practice by emphasising the importance of procedures which to the layman are *scientific*.

Many patients are fated to suffer from ailments requiring treatment for an indefinite period. Thankfully the novelty of such treatments soon wears off, and they are taken as a matter of course (like teeth-cleaning and shaving). One seldom meets a " glycosuria neurosis " in a diabetic, or a " hæmoglobin neurosis " in a patient with addisonian anæmia, for instance.

Hypochondriasis is socially boring, and economically disastrous to the patient (if, at times, profitable to medical practitioners). All practitioners interested in the happiness of their patients should be on their guard against producing it.

Barton-on-Humber, Lincs. S. H. F. HOWARD.

NOT FOR SALE

SIR,—It is indeed high time that the issue raised in your leader of Jan. 14 was tackled. I refer to the insidious undermining of the N.H.S. by a few individuals who, now as " independent contractors " (or private doctors) and now as employees of the community, get the best of both worlds and spoil it for the rest. Or the lie given to what is a slander if it isn't the truth. As a general practitioner I have found time and time again just how widespread such a belief is both amongst the public and colleagues.

If abuse there is it is most important to effect a change before it becomes a political issue—that is, before non-professional forces are brought to bear. In this I believe that our democratic organisation and professional freedom can achieve results.

In the General Medical Services there is already a mechanism for reviewing patients who are on the " panel ": a slight extension of this to the hospital service with special note of the waiting-time and route of entry into hospital would have a most salutary effect if abuse there is, and if not it would still be a valuable study into the working of the hospital service.

Moseley, Birmingham. B. BARNETT.

PRIVATE PRACTICE

SIR,—Your correspondent in the Widdicombe File (Jan. 14) is, I think, losing sight of the ethical position of our profession. His letter may be reduced to: " I will not see patients privately because I do not like doing so." Surely it is our duty to serve our patients coming to us in the proper way, through their family doctor, as they desire. If they desire to have our opinion through the National Health Service we must give them as good a service as lies in our power. If they desire to see us privately it is our bounden duty to make ourselves available to them in that way. We may not sit in judgment and lay down rules as to how we are to serve.

London, W.1. A.. F. RUSHFORTH.

TREATMENT OF DRUG ADDICTION

SIR,—Lady Frankau's letter of Jan. 21 repeats much of what appeared in her article on the treatment of addiction but evades the question I posed (Jan. 7)—namely, how many of her 32 cases have relapsed since she successfully cleared them of dependence on drugs?

I use the term "evade" expressly because she writes: "Only 1 patient in this series has relapsed and *not returned for treatment* " (my italics).

If Lady Frankau's technique of treatment and management reduces the liability to relapse it should be widely publicised. But this has not yet been established.

She states that in her experience patients who " relapse " do so within days and weeks rather than months. I personally would not regard a patient who only managed to keep off his drug for " days " as having successfully completed treatment. Yet one must assume that such cases are included in Lady Frankau's series because no period of time is mentioned before which the claim of " cleared of dependence on drugs " is not made.

It may well be her experience that addicts who have served prison sentences relapse almost immediately after release. But what I said was that certain types of addict are rarely cured outside prison.

It is difficult to reconcile Lady Frankau's statement that addicts reporting for treatment minimise the amount of drugs

they are taking with her assertion that " intensive psychotherapy helps the patient to acquire insight . . . and finally to avoid the temptation to augment his income by selling drugs ". How can they have any drug to spare if they minimise their requirements?

Lady Frankau has conceded that some of her former patients do not return for treatment after relapse. May I inquire how she can be satisfied that those others who do not return are still free of dependence on drugs?

London, W.1. ELLIS STUNGO.

NO CHAIR

SIR,—I was interested in Dr. Spencer's letter (Jan. 7) on the absence of a chair in psychiatry in Birmingham. The same unfortunate state of affairs exists in clinical infectious diseases. Except for Glasgow, there is no chair in the *whole* of the British Isles! It is true that some holders of general medical chairs—notably Prof. C. H. Stuart-Harris—have both taken an interest and made fundamental contributions to knowledge in this field. Apart from them, however, little or nothing has been done, possibly because of apathy, indifference, professional jealousies, and the competing claims of general medicine and pædiatrics.

There is no doubt that an active chair stimulates the growth, development, and prestige of a specialty, just as the presence of a queen bee is essential to the well-being of a hive! It is all the more surprising that some charitable foundations have not come forth with offers of financial help.

Competing claims of other equally pressing and just causes may well be put forward. Perhaps, if an approach could be made by influential lay or medical people, something might yet be achieved for both our specialties.

Romford, Essex. I. M. LIBRACH.

DEATHS UNDER DENTAL ANÆSTHESIA

SIR,—Dr. Butler's letter (Jan. 14) raises three vital issues in outpatient anæsthesia—viz., the safety of trichloroethylene, adequate oxygenation, and fainting in the dental chair.

The use of any potent adjuvant in the presence of inadequate oxygenation has long been recognised as dangerous. McConnell [1] expressed this in relation to trichloroethylene, and I would go further and suggest that this agent cannot be regarded as " unquestionably safe " under whatever conditions it is used. In an account of 1000 deaths associated with anæsthesia, Edwards [2] reports 12 with trichloroethylene. 3 were attributable to overdosage, and the remaining 9 were thought to have resulted from " primary cardiac failure ". Having reported one of these latter cases myself I am convinced that this is a real hazard, which can be minimised only by the preoperative use of atropine and adequate oxygenation.

Being actively concerned with the teaching of dental anæsthesia I am distressed to read that dental outpatients are " regularly subjected to oxygen concentrations as low as 5% ". While it is perfectly correct to emphasise the increased hazards introduced by the addition of adjuvants to anoxic mixtures, surely nowadays the use of such anoxic mixtures in themselves should be universally recognised as physiologically unsound. That nitrous oxide can be effective even when used with an adequate oxygen supply has been recognised by Tom [3] and Mostert [4] and can readily be demonstrated provided the signs of third-stage surgical anæsthesia are not expected. Where this light level of anæsthesia will not suffice, I agree with Dr. Butler that halothane, especially if administered from a Goldman vaporiser, is preferable to the use of any other adjuvant.

That fainting can occur in the dental chair is well recognised by those who only employ local anæsthesia. I have observed fainting on more than one occasion, in susceptible people, during the recovery period after general anæsthesia when the danger is that it may be unrecognised and the patient left sitting upright.

Fainting during a general anæsthetic in the dental chair is another matter. I believe that, by definition, the existence of the condition cannot be proved. If, however, the accompanying physical signs appear, for safety's sake the condition should be regarded as a circulatory collapse in response to the anæsthetic technique and appropriate treatment commenced forthwith.

Finally may I point out that, as there are more general anæsthetics given in this country for dental surgery than for all other types of surgery, there is a widespread need for postgraduate courses of instruction in dental anæsthesia, which at present are available only in London. These must be comprehensive and available to all who are concerned in the administration of dental anæsthetics—i.e., to doctors and dentists alike. In this way our two professions can cooperate to improve the service to the patient.

Dental Hospital, Manchester. T. DINSDALE.

1. McConnell, W. S. *Proc. R. Soc. Med.* 1959, **52**, 323.
2. Edwards, G., Morton, H. J. V., Pask, E. A., Wylie, W. D. *Anæsthesia*, 1956, **11**, 194.
3. Tom, A. *Brit. med. J.* 1956, i, 1085.
4. Mostert, W. J. *ibid.* 1958, i, 502.

PSYCHIATRIC ASPECTS OF ACUTE PORPHYRIA

SIR,—Dr. Cashman's letter (Jan. 14), describing two cases of acute porphyria, raises again the question of the true incidence of the condition in this country. It also reiterates the need for constant awareness, particularly amongst psychiatrists, of the presenting features, which may fall into a well-defined pattern as is illustrated by the following case-record.

The patient, a single woman of 44, was first admitted to a mental hospital in April, 1959, complaining of weakness, pain in the abdomen, shoulders, and arms, and depression. The results of physical examination were entirely normal except for a hæmoglobin level of 74%. Hysteria was diagnosed. She received sulphonamide therapy for a heavy urinary infection, which cleared up quickly, but was given no other medication. She rapidly ceased to complain and was discharged symptom-free.

Her previous medical history included nine admissions to general hospitals since 1938. On each admission she had complained of abdominal pain, sometimes generalised, on two occasions starting in the loin. Investigations had included barium-meal examination, intravenous pyelography, and cystoscopy. The diagnosis arrived at had varied with each admission and had included duodenal ulcer, neurasthenia, dysmenorrhœa, urinary infection, pyrexia of unknown origin, osteoarthritis of the spine, renal colic, and chronic hysteria.

Her mother had died in 1938 of a wasting disease. The cause of death was given as chronic bulbar palsy. It was noticed at home during the last illness that the mother's urine was dark and stained the sheets, and urine-testing during the two days she spent in hospital showed the presence of urobilinogen. One brother had died in 1957 of pneumonia and was found post mortem to have complete situs inversus. There are four other siblings, none of whom has any similar illness.

Two weeks after discharge the patient was readmitted to this hospital complaining of weakness and depression. Once again no abnormality was found, but her urine was port-wine-coloured and contained porphyrins. Acute porphyria was diagnosed, and the urine of all known relatives was tested for porphyrins. Traces of porphobilinogen were found in the urine of two nephews, neither of whom had ever had symptoms of the disease.

This case illustrates well three aspects to be borne in mind in making the diagnosis:

1. The triad of presenting features described by Cross [1]—abdominal pain, paralysis, and psychic changes. On each of

1. Cross, T. N. *Amer. J. Psychiat.* 1956, **112**, 1010.

her many hospital admissions the patient had complained of abdominal pain. The weakness she described was confirmed by her father, with whom she lived, and is probably a manifestation of transient paralysis. The psychic changes presented as depression and also led to the diagnosis of hysteria.

2. Family history of the disease. While we cannot assume that the mother died of acute porphyria, the evidence is very suggestive. The two nephews have latent porphyria.

3. A multiplicity of misdiagnoses extending over many years.

There remains the question of incidence. Routine screening of hospital admissions would be simple to arrange, and in fact all patients admitted to this hospital have their urine tested for porphobilinogen by the Watson and Schwartz [2] method.

I wish to thank Dr. J. P. Spillane for permission to describe this case and for his interest and encouragement.

Whitchurch Hospital, Cardiff. K. MYERS.

SIR,—Dr. Cashman's letter prompts me to report another case of acute porphyria first diagnosed at a mental hospital.

An unmarried woman of 20 presented with colicky abdominal pain and vomiting and subsequently, in February, 1960, underwent exploratory laparotomy and appendicectomy. Since the pain and vomiting recurred 6 weeks later she was readmitted to another hospital, where, in the absence of an apparent organic cause, a psychiatric opinion was sought. Her history revealed that she had always been shy and had had difficulty in mixing, that she disliked any show of affection, and was extremely embarrassed about sex; there had been recent differences with a boy-friend; and her mother, after a stillbirth, had had a period of nervousness and depression and difficulty in swallowing. Her symptoms were thought to be hysterical and she was treated as a day-patient at Goodmayes Hospital along group psychotherapeutic lines. Physical examination (April, 1960) showed a lightly built young woman who seemed underweight, had unusually dark skin, a tachycardia of 100, and a keloid recent right paramedian abdominal scar.

For the first week she seemed to improve but then began to deteriorate. She often said she had abdominal pain and felt weak, would slump to the floor and scream for her mother. On May 24 she developed bilateral wrist-drop and was admitted to the main hospital. She had a tachycardia of 140 and bilateral wrist-drop, but fairly good power elsewhere, though the tendon jerks were sluggish. On May 26 she complained of difficulty in swallowing; on May 29 intermittent aphonia was present, and in the early hours of May 30 she was incontinent of urine. Next day she had gross weakness of both upper and lower limbs, aphonia, difficulty in swallowing, and lower intercostal paresis. She was therefore admitted to a poliomyelitis unit where she died 18 days later.

Investigations.—April 28: Chest X-ray normal; erythrocyte-sedimentation rate 2 mm. in 1 hour; Hb 98%; W.R. and P.P.R. negative. May 30: white count 7800 per c.mm., no basophilic stippling. Urine: normal colour, darkened to a brownish-red over 24 hours and more rapidly on addition of HCl; Waldenström's test for porphobilinogens positive, Rimington's test positive, amyl alcohol extract of urine gave a marked pink fluorescence with ultraviolet light.

The association of colicky abdominal pain with wrist-drop led to tentative diagnoses of lead-poisoning or acute porphyria on May 25. Sodium amylobarbitone was prescribed as a night sedative on May 24, but no barbiturates had been prescribed at the hospital before this. On May 27, when asked to take her own tea, she screamed for half an hour and accused the sister of feeding her with boiled fish and a doctor of hitting her. Questioned about her urine on May 31, she said that it had been a peculiar dark colour on and off since her appendicectomy.

This case illustrates several well-documented features of acute porphyria, and also some of the pitfalls to which the diagnostician is commonly led. The presenting symptom here is manifestly non-psychiatric and even the so-called hysterical behaviour is best explained as a normal reaction to painful and disabling symptoms together with exasperation at others' incredulity. Prunty [1] suggests that acute porphyria is not as rare as is commonly thought. Once the diagnosis is seriously considered, confirmation is relatively easy.

I thank Dr. J. E. McA. Glancy and Dr. R. C. Gledhill for permission to publish details of this case.

Goodmayes Hospital, Ilford, Essex. I. G. PRYCE.

2. Watson, C. J., Schwartz, S. *Proc. Soc. exp. Biol., N.Y.* 1941, **47**, 393.

THE OXFORD CLINICAL SCHOOL

SIR,—Much of the factual information contained in the letter (Jan. 7) from "Anonymous Cantab." under this heading is happily now out of date, although it has only recently become so. But a disturbing point about the letter is that it blurs the distinction between, on the one hand, the arrangements at Oxford for admission to colleges of school-leavers intending to read for medical degrees, and, on the other, the arrangements for clinical teaching at the United Oxford Hospitals. It would be most unfortunate if these were to become confused in the minds of those who may have to advise young people on the choice of a university. Your own annotation [2] a few weeks earlier did avoid this particular misconception although it might be faulted on other grounds.

OXONIENSIS.

DRUG TREATMENT OF DEPRESSION

SIR,—Since I have been concerned with both clinically and experimental aspects of amine-oxidase inhibitors for several years, I was extremely interested in the two articles (Jan. 7) on the comparison of results obtained with monoamine-oxidase inhibitors in the treatment of depressive illnesses.

Crisp, Hays, and Carter found "no significant differences in the clinical results" obtained with iproniazid, pheniprazine, and nialamide. Dally and Rohde obtained greater improvement with iproniazid than with isocarboxazide, phenelzine, pheniprazine, and nialamide. A divergence of opinion regarding the relative toxicity of these compounds was also expressed. It is difficult to reconcile the conclusions reached by these two groups of investigators because of the nature of their reports. Crisp et al. stated that "the mean difference between initial and final measurements of serum-glutamic-oxaloacetic transaminase, serum-bilirubin, and thymol turbidity for the three drugs [iproniazid, pheniprazine, and nialamide] did not differ significantly". Yet in the accompanying table they mark that these drugs do vary, according to these tests, in the ability to produce "deterioration of liver function". But I would like to know why both the mean changes of 3·6 units and 0·17 units in the serum-glutamic-oxaloacetic-transaminase levels should indicate "a deterioration of liver function", whereas an intermediate mean change of 0·25 units does not. Likewise it is difficult to comprehend why a change of 0·08 thymol-turbidity units indicates decreased liver function and the greater change of 0·11 units does not. I must also question the statement that the effect of nialamide on serum-glutamic-pyruvic transaminase "was not significantly different from iproniazid", whereas the table indicates that there is about a 6-fold difference in the changes produced by these drugs. The conclusion that pheniprazine produces less "derangement of liver function" than nialamide does not appear to be justified on the basis of the data which they presented.

Comparison of the therapeutic results obtained by Crisp et al. and by Dally and Rohde with monoamine-oxidase inhibitors is difficult, since the methods which the latter investi-

1. *Medical Annual*, 1952; p. 293.
2. *Lancet*, 1960, ii, 1336.

gators employed are not clearly presented. The means and criteria for evaluation of the therapeutic response are not mentioned, but presumably neither single-blind nor double-blind tests were employed. Therefore, it is not surprising that "the results also confirmed . . . [their] clinical impressions", since these results were apparently based on these impressions. Of greater importance, however, is the fact that the inclusion in the experimental group of "43 patients who were all [previously] known to respond well to iproniazid" introduces considerable bias in favour of this drug, and it would indeed be surprising if under these circumstances it did not "appear" to give the best results. With such bias, the results obtained with the Chi square test or other statistical methods are of little practical significance. The experimental design is not apparent from the description of the methods or from the data presented. Apparently, however, an incomplete cross-over technique was employed. This may possibly account for the discrepancy between their results and those of Crisp et al.

A survey of over 300 publications on the efficacy of monoamine-oxidase inhibitors indicates that, in appropriate dosage, the therapeutic effectiveness of these compounds is similar, with improvement occurring in approximately 50–80% of patients. An analysis of the toxicity and side-effects confirms, in general, the findings of Dally and Rohde, indicating that side-effects are "commonest with iproniazid and rarest with nialamide".

Department of Pharmacology, University of Hong Kong. CARL C. GRUHZIT.

PROPRIETARY NAMES OF DRUGS

SIR,—Those of us who attempt to keep up with new developments in medicine and chemotherapy certainly have reason to sympathise with Professor Wade (Jan. 21). However, these seemingly annoying differences in describing a given drug are often caused by difficulties in registering the same trademark in different countries.

London, W.C.1. G. A. SCHMEIDLER.

IS RADIOLOGICAL EXAMINATION OF A TWISTED ANKLE NECESSARY?

SIR,—As a radiographer and a radiologist of over 40 years' experience, my emphatic answer to this question is No; and I base this opinion on the teachings of those leaders I profess to follow—Hugh Owen Thomas and Sir Robert Jones, who contributed more to orthopædic treatment than all the other doctors since Hippocrates. Their success was based on sound clinical treatment. I cannot therefore agree with Mr. Rowland Hughes' quotation (Jan. 7) that "radiological control is the basis of all good treatment of sprains". Doctors who work on such a basis may do harm and subject their patients to unnecessary fear and pain.

A man who had sprained his ankle was sent to my department by an accident surgeon. The radiographs showed a linear fracture of the lower third of the fibula, but no other change, and no displacement. I duly reported these findings. A week later the patient came for a further examination because his clinical condition had markedly worsened. I reported that the new radiographs showed a complete dislocation of the ankle-joint and obvious displacement of the fibula fragments. The surgeon asked for confirmation of my original report, and, on my repeating this, he asked whether the soft tissues might not have been severely damaged by torsion. I frankly admitted this. Was it the radiographic interpretation or the clinical interpretation which was at fault? In the hands of a sound general practitioner without ready access to an X-ray department, the clinical condition would have been duly recognised, and the catastrophe would not have happened. Apparently the good position of the bones in X-ray had dictated the treatment and not the clinical condition—hence the displacement.

A friend of mine tripped on the stairs and injured her ankle. Her general practitioner could not detect a fracture or displacement but insisted that the ankle be supported by a bandage, and the patient remain in bed for as long as the ankle was painful. By chance I called to see her; and she told me that the doctor was going to take her to hospital next day for an X-ray if the pain persisted. To save her the trouble, I fetched my portable X-ray apparatus, and a simple linear fracture of the lower third of the fibula was revealed. Her doctor decided to keep her in bed with a stiff bandage on the ankle and to forbid weight-bearing until her pain had ceased. In other words he continued the treatment he had started and would have continued if no X-ray had been available. The patient, having been disturbed as little as possible and not subjected to unnecessary apprehension and pain, made a complete recovery, and within a month was back at her household duties.

Many such instances will be found in my book [1]; and more recently I referred to a series of such cases.[2] Many doctors would have no difficulty in recollecting similar instances among their own patients.

Birmingham. JAMES F. BRAILSFORD.

THE GENERAL PRACTITIONER AND THE HOSPITAL

SIR,—Dr. Chapman (Jan. 14), writing about the general practitioners in hospital, says that after some early misgivings the consultant staff, he thinks, are satisfied with the general practitioners. Having worked in that hospital for many years, I have never been conscious of any misgivings, and I think that would be the opinion of my colleagues. The standard of work is extremely good, and in a hospital of this size I am sure that the system of general-practitioner clinical assistant is the only satisfactory one.

Hull. D. C. MUIR.

TEACHING IN GENERAL PRACTICE

SIR,—In his interesting article of Jan. 7 Dr. DeLacey draws attention again to the fact that medical students can get little experience of many conditions common in general practice, and are increasingly taught by consultants with no personal experience of looking after patients in their homes. Many think that this can be remedied by attaching students to general practitioners for short periods of time.

It is, however, important to ask which of two purposes one wishes to accomplish in so doing.

The first is that of giving clinical teaching on illness as seen in general practice, and instruction in the administration and organisation of a general practice.

The second is that of using the conditions of general practice to enable the student to see patients as people rather than "cases", as individuals with homes, jobs, and a unique physical and psychological environment.

The first aim can really be justified only if one intends to train all students as possible general practitioners, and there are a number of serious additional criticisms that can be made. The most relevant objection is that general practice is a special field of medicine, and like any other specialty cannot properly be studied until basic medical training is completed. The student has an opportunity for study of the principles of the medical sciences which few will have again after qualification, and anything which interrupts or diminishes such opportunities is to be avoided.

There are, however, good reasons for bringing all students (whatever medical career they aim at) into general practice, there to see illness in its social setting, to see sick people as individuals, and to grasp the relationship between prognosis,

1. Brailsford, J. F. The Radiology of Bones and Joints. London, 1953.
2. *J. int. Coll. Surg.* 1960, **34**, 267.

treatment, and prevention on the one hand and the environmental factors on the other. Such experience cannot fail to be of value to every student, because the final concern of every doctor is the human individual.

Belfast. R. P. MAYBIN.

SURGERY OF PAINFUL HIP

SIR,—I read Mr. Nesfield's letter of Dec. 17 with interest.

As the classical indication for surgical intervention in osteoarthritis of the hip is pain, and also with the almost general acceptance of McMurray's displacement osteotomy as the best operation, I am persuaded to think that division of the gracilis tendon at its origin achieves the same object as osteotomy in relaxing the shortened muscle in spasm.

I should very much like to know if Mr. Nesfield has found any evidence of regression of radiological features in painful osteoarthritic hips.

Roehampton, London, S.W.15. J. A. THETHRAVUSAMY.

EXTERNAL CARDIAC MASSAGE

SIR,—May I reply to the critics (Jan. 21) of the method of "external cardiac massage"? Both appear to have overlooked several points:

(1) As long as the heart-valves are intact, irrespective of pressure differentials, compression of the heart must force blood into the aorta.

(2) I do not think this type of massage can be compared with a "gentle flick" of the finger as it requires quite violent exertion.

(3) Use of the word "successful" was intended to imply that it was a practicable method of restoring circulation. The patient, in fact, died of multiple cerebral emboli.

(4) I am familiar with Dr. Bullough and Dr. Rainer's contribution and would repeat that this was the first case reported using the Baltimore method. I am sorry if they have misunderstood me over any claim to priority.

(5) Neither the surgeon concerned, the registrar, nor I thought that thoracotomy was indicated in this particular case.

I should hope that readers of this correspondence would not assume that thoracotomy for cardiac arrest is to be deprecated. On the contrary, when facilities exist it is the first method of choice. I would reiterate that there are circumstances when opening the chest is impracticable and when this system of massage will allow suitable preparations to be made while an adequate circulation is maintained, irrespective of asystole or ventricular fibrillation.

Guy's Hospital, London, S.E.1. P. J. MOLLOY.

HOSPITAL INFECTION

SIR,—Your editorial[1] and 3 subsequent letters[2–4] suggest that in our book *Hospital Infection* the need for refrigerated ventilation in operating-theatres is underestimated.

It is surprising that none of your correspondents complaining of excessively high temperatures and humidities in their theatres has anything to say about the siting of sterilising equipment in relation to the operating-room itself. The conditions complained of by Mr. Murley could surely have been produced only by the presence of steam in the atmosphere.

The paragraph in our book (p. 168) which has been criticised contains the sentence: "Unlagged sterilisers, boilers without simmering controls and sterilising rooms with open communication to the theatre are the main and avoidable reasons why so many surgeons in temperate climates have to work in subtropical conditions." Elsewhere (p. 163) we emphasise that the sterilising-room should be entirely separate from the theatre, and (p. 170) that there should be no airflow between them. At least in designing a new theatre it is surely better to control the liberation of heat than allow it to be liberated and then try to remove it by refrigerated ventilation.

R. BLOWERS
L. P. GARROD
R. A. SHOOTER
R. E. O. WILLIAMS.

1. *Lancet*, 1960, ii, 1235.
2. Murley, R. S. *ibid.* p. 1346.
3. Aiken, D. *ibid.* Jan. 7, 1961, p. 53.
4. Arden, G. P., Maudsley, R. H. *ibid.* p. 54.

NORMALCY AND THE GAMMA EFFERENT SYSTEM

SIR,—We wish to congratulate Dr. Menkes for his concise treatment of the complex subject of the gamma efferent system in your Very Special Article (Dec. 24). While agreeing with most of the sentiments expressed, we beg to differ on one major point: the assumption that disproportionality between input and outflow of the gamma efferent system is responsible for deviations from normalcy, as for example in beatniks, is totally unwarranted. Following the original graphic description of Greenwich Village Beatnik Life and Thought,[1] we have made intensive biochemical and pharmacological investigations and our findings[2] show that the answer is not as simple as that suggested by Dr. Menkes. It seems probable that further chromatographic studies using C^{14}-labelled progesterone[3] may shed some light on the derangement of metabolism which must be the basic abnormality affecting conductivity of the gamma efferent system.

As for the article by J. Lilly, we found the opinions interesting but were unable to find the reference, even though we ourselves attended a round of cocktail parties in the medical communities of Boston and New York recently. Was it possible that in the process of modulating the sensory impulses at these parties we failed to register his name centrally, or could the action of ethanol on antidromic impulses in the cortex have played a greater role?

Furthermore, we were unable to trace other references given, among them J. Strauss on Wine, Women, and Song. A publisher informs us that a musical score by this name is available, but it is possible that the publisher of the book and year of publication were not given in the reference because the book is not yet off the press.

Another serious omission in the article was the author's address. We tried to obtain a reprint of the paper from Johns Hopkins but could not trace the author's name at that august institution. Has the author been so busy recently that he has forgotten to modulate his motor outflow and thus has failed to inform the relevant authorities of recent movements, even if these are somewhat incoordinate?

We hope that this letter will not be considered as a personal attack[4] on Dr. Menkes, for we can only progress by criticism and repeated self-examination,[5] as in a negative feedback mechanism.[6] We look forward to a reply and to many more articles from Dr. Menkes in this fascinating field.

Departments of Pharmacology and Psychiatry, Cornell University Medical College, New York. EDEL BERMAN CRAIG BURRELL.

1. Pfeifer, Jule. *The Observer*, Nov. 24, 1960, as reprinted from *The Villager*, March 7, 1960.
2. Berman, E., Burrell, C. D. *Acta biochim.* (*N.Z.*) **9**, 473.
3. Bligh, E. G. et al. *Arch. Biochem.* 1955, **158**, 249.
4. Searle, Ronald, drew a cartoon in *Punch*, Feb. 19, 1959, entitled "How to leave footnotes in the sands of time, when wearing beatnik sandals". In our opinion, too much attention has been paid to the psychoanalytic condition of the subjects in the cartoon: rather, they should be taken at face value.
5. Eisenhower, Dwight D. Speech at the Summit Conference, Paris, 1960. As quoted in *Izvestia*, May 17, 1960.
6. Answer obtained on an I.M.B. 705 computer on feeding the necessary information into it ($P < 0.05$; all variables kept constant for the duration of the experiment).

SIR ARCHIBALD McINDOE, 1900-1960

Mr. LEONARD MOSLEY writes:

"I have been commissioned by his family and executors to undertake the authorised biography of the late Sir Archibald McIndoe. I would be most grateful if anyone in possession of personal letters or recollections would communicate with me, c/o Weidenfeld & Nicolson, Ltd., 20, New Bond Street, London, W.1."

Obituary

KENNETH ALEXANDER INGLEBY-MACKENZIE
K.B.E., C.B., B.A., B.M. Oxon.

Surgeon Vice-Admiral Sir Alexander Ingleby-Mackenzie, a former medical director-general of the Navy, died on Jan. 17 at the age of 68.

Elliott & Fry

He was the elder son of Dr. K. W. Ingleby Mackenzie, who practised in the Isle of Wight. He was educated at Repton, Trinity College, Oxford, and St. Bartholomew's Hospital. After qualifying in 1916 he entered the Royal Navy as a surgeon lieutenant. Between 1917 and 1919 he served in H.M. Ships *Coledin* and *Cardiff*. In the latter he was in action in the Heligoland Bight in November, 1917, and gave valuable help with the treatment of the wounded. Between the two wars he specialised in medicine, and twice served at the Royal Naval College, Dartmouth, was on the staff of the P. and R.T. School, Portsmouth, and was also fleet medical officer of the East Indies Squadron. He was promoted surgeon lieut.-commander in 1922 and surgeon commander in 1928. In 1935 he retired from the Navy at his own request with the rank of surgeon captain, intending to take up a different career, but he rejoined the Service two years later.

At the beginning of the late war he served in H.M. Ships *Resolution* and *Royal Sovereign* in the Home Fleet. After two years at the Royal Naval sick quarters at Dartmouth he joined the Naval Hospital Ship *Vita* and took part in the landings at Sicily and Italy. Later the ship proceeded to the Far East and he became fleet medical officer, Eastern Fleet. In 1944 he was appointed in charge of the medical section of R.N. Hospital, Haslar, and two years later he became principal medical officer of R.N. Barracks, Chatham. In 1948 he was promoted surgeon rear-admiral and appointed medical officer in charge of the Royal Naval Hospital, Chatham, and command medical officer to commander-in-chief, The Nore. He was appointed C.B. in 1951, and the following year he became medical director-general of the Navy. He was appointed K.B.E. in 1953 and placed on the retired list in 1956. After retirement he became assistant managing director of Arthur Guinness, Son & Company, Ltd.

A colleague writes:

"It was early recognised in the R.N. Medical Branch that Alexander Ingleby-Mackenzie would go a long way, for his outstanding characteristics were his immense enthusiasm and drive, and he never spared himself. He was a first-class games player and had captained the hockey team at Oxford, but was almost equally good at golf, tennis, or squash. His appointment as medical director-general was warmly welcomed throughout the Service, and his four years' tenure of office was highly successful. His appointment to Arthur Guinness showed how highly he was thought of outside the Service. He will be remembered as a very pleasant person who loved both work and games, and he was a very pleasant messmate. He was always willing to give sound advice or a helping hand to all who asked for it."

Sir Alexander leaves a widow, two sons, and a daughter.

IAN McCRACKEN
M.A., M.B., B.Sc. Glasg., D.P.H.

Dr. Ian McCracken, who was for over twenty years medical officer of health for Co. Durham, died on Jan. 6 at the age of 63.

The son of the late Rev. McCracken of Burntisland, Fife, he was educated at Whitehill School, Glasgow, and at the University of Glasgow. After graduating in arts and in science, he continued his training in medicine at the same university, qualifying in 1924. After holding house-appointments in Glasgow hospitals he joined the city's public health department, where he served as tuberculosis officer and divisional medical officer. In 1937 he moved to Durham as deputy to the county medical officer, and the following year he was appointed county medical officer. He held this post until his retirement in 1959 because of ill health.

G. W. writes:

"Studious, careful, and thorough by nature, Ian McCracken applied these qualities to great effect in carrying out the onerous duties of his post. His decisions were given only after consideration of all factors—factors which his orderly methods of thought enabled him to grasp and assess with sure judgment. In debate he preferred to await a request for his opinion, and when that came, as it surely would, his views were given clearly and with a characteristic economy of words. Essentially he was a scholar, Greek (he read from the original) and mathematics being among his recreations and he used his leisure in retirement to study Russian. While these features give a guide to his character, those who knew him will remember most his ready sympathy and interest, and above all his complete integrity and sense of purpose."

A. K. MacR., a friend from school and university days, writes:

"Intellectually, Ian McCracken was on a plane above most, being a brilliant mathematician and student of the classics. Throughout his many scholastic successes he remained modest and unassuming, and this may have been one of the reasons of his popularity with us all. On first acquaintance his manner was reserved, but, with greater intimacy, this reserve readily broke down to reveal a pretty wit, a keen sense of humour, and a refreshing vivacity. There were few with whom one could spend an evening as pleasantly as with Ian McCracken. As host or guest he was thoughtful, courteous, and considerate. It was obvious that those who had worked with him over the past twenty-one years in Durham held him in high regard, conscious of his erudition and culture and admiring his loyalty and integrity."

Dr. McCracken leaves a widow.

EDWARD THOMAS MEAGHER
M.R.C.S.

Surgeon Rear-Admiral Meagher, who died on Jan. 13 at Tunbridge Wells, served as a visiting commissioner of the Board of Control after his retirement from the Navy. He was 90 years of age.

He was educated at St. Bede's College and the Victoria University of Manchester, qualifying in 1891. The following year he joined the Royal Navy and served on the China station. During the Spanish-American war he acted as interpreter with the Spanish fleet in Manila Harbour. Later he was posted to the Royal Naval Hospital at Malta and to H.M. dockyard, Haulbowline. In 1912 he was appointed to

H.M.S. *Cumberland* in which King George VI, then Prince Albert, made a training cruise as a cadet.

During the 1914–18 war Admiral Meagher served in the Cameroons and was later in charge of the Royal Naval Hospital, Yarmouth, a hospital for the treatment of mental disease. In 1920 he was naval representative on the Shell Shock Commission which met in Vienna. He retired from the Navy in 1925, and the following year was appointed as an inspector of the Board of Control. Almost at once he began a study on general paralysis and its treatment by induced malaria. At that time the disease was responsible for some 1500 deaths annually in this country. The results of his investigation were published in 1929 in a report sponsored by the Board; it included information from this country and from many European clinics which he visited. He later became a commissioner of the Board. A man of independent mind, and a great worker, deeply interested in the hospitals and the patients, he is remembered by his colleagues with respect and affection.

Admiral Meagher married in 1908 Dorothy, daughter of Commander A. E. McMurdo, who survives him with two sons and five daughters.

JULIUS ENGELBRETH-HOLM
M.D.

Professor Engelbreth-Holm, who held the chair of pathological anatomy in Copenhagen and was an international authority on the neoplastic diseases, especially leukæmia, died in the Middlesex Hospital on Jan. 17 at the age of 57. Though his health had been poor in recent years, he had come to London for a meeting of the European scientific advisory committee of the Lady Tata Memorial Trust, with which he had been associated since 1934, and of which he became a member after the late war.

F. H. K. G. writes:

" Engelbreth-Holm made many contributions to knowledge of the avian and mammalian leukæmias, and he led and inspired a team of active workers in these fields at the Fibiger laboratory in Copenhagen. In this country he will be most widely remembered as the author of the book, *Leukæmia in Animals*, written at the request of the Tata Committee, to survey the existing knowledge of the subject up to 1940. The manuscript of this book, with an English translation by the late Mr. C. L. Heel, was smuggled out of Denmark at the start of the German occupation; and it was my privilege, as the then secretary of the Tata Committee, to edit it for publication in England in 1942. I had first met the author when, as a young grantee of the Lady Tata Trust, he came to London, with his wife, for the second International Congress for Microbiology in 1936; and we had been firm friends ever since. He was a delightful companion, with wide scientific and cultural interests, and he will be sadly missed by colleagues all over the world."

Appointments

COWIE, R. S., F.R.C.S.E., F.R.F.P.S.: part-time consultant orthopædic surgeon, Shrewsbury hospital group, and the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry.
GRANT, J. D., M.B. N.U.I., D.P.H.: assistant M.O., Surrey.
SCHLEYER-SAUNDERS, EMANUEL, M.D. Vienna: hon. consultant gynæcologist, Italian Hospital, London.
SMITH, W. D., M.B. Glasg., D.P.H.: assistant M.O., Surrey.

East Anglian Regional Hospital Board

BANERJEE, GOUTAM, M.B. Utkal: orthopædic registrar, Peterborough hospital group.
CHAMPION, R. H., M.B. Cantab., M.R.C.P.: consultant dermatologist, United Cambridge Hospitals, and East Anglian Regional Hospital Board.
KIRK, A. G., M.R.C.S.: registrar in psychiatry, St. Andrew's Hospital, Norwich.
PRICE, M. W., B.M. Oxon.: registrar in psychiatry, Fulbourn and Addenbrooke's hospitals.

Notes and News

HOW MUCH FOR HEALTH?

THE review of the economic situation prepared by the information division of the Treasury contains this month [1] an analysis of expenditure on social services by all public authorities (central Government, National Insurance Funds, and local authorities).

In 1959 expenditure on social services (current and capital combined) was 89% higher in money terms and about 40% higher in real terms (allowing for price increases of about a third) than in 1950. National income over the period increased by 77% in money terms and about 20% in real terms. As a proportion of national income at factor cost, expenditure on social services, after falling from 18·1% in 1950 to 17·5% in 1954, edged up to 19·4% in 1959. The rise was entirely due to higher current spending: the share of capital spending in national income fell from 3·3% in 1950 to 2·4% in 1959. The ratio for the health service's current spending to national income was 4·3% in 1950, 3·6% in 1954, and 4·0% in 1959.

The main changes in the pattern of current spending of all the social services have been rises in the share of National Insurance (particularly in retirement and widows' pensions) and education and a fall in the share of the National Health Service. The share of the N.H.S. reached a peak in 1950–51 (28·5%) and then declined, following the introduction of charges for certain services and a general charge for prescriptions. Expenditure in 1959–60 was £775 million, or 23·1% of the total.

Capital expenditure in 1959–60 (£446m.) was about an eighth of all social-service spending; the proportion was about a third smaller than in 1949–50. Housing construction by local authorities accounted for 78% (£262m.) of the total in 1949–50, falling to 56% (£249m.) in 1959–60 as private building expanded. This decline was offset by a rapid rise in the share of education from 11% to 33% and a slight rise in the share of the N.H.S. from 7% (£23m.) to 8% (£36m.).

SHORTAGE OF HOSPITAL MIDWIVES

THOUGH the number of midwives in the National Health Service is gradually rising there are still not enough for immediate or future needs. The shortage would be almost met if every woman who qualified practised midwifery for at least a year; but at present only half of those who qualify practise at all, and of these only half are still in practice three years later. The need is thus not only for a persistent recruiting drive but also for action to remove the midwife's unwillingness to practise her speciality, and the Minister of Health has suggested to hospital authorities possible means.[2]

The memorandum points out that of 70,000 women on the Midwives Roll about 20,000 have ceased to practise, usually for domestic reasons. Many of these might return to work if working conditions and hours of duty could be arranged to suit their circumstances. This might mean an adjustment of ward procedures. For instance, the time at which beds are made might need to be altered. Women who return to midwifery are required to take a refresher course, but in areas where the shortage is acute the Central Midwives Board is prepared to postpone this requirement. The memorandum also points out that training in midwifery is not restricted to registered nurses and suggests that useful recruits might be found among older women who wish to take up a new and satisfying career, perhaps after their families have grown up. Not all needs can be met if recruitment is restricted to those with grammar or technical school training.

In the hospital every effort must be made to use midwives economically. In these days of early ambulation a mother soon gets up and can reasonably be expected to attend to some of her personal needs herself. " Rooming-in " can also relieve the midwife of some work, for the mother can provide much

1. *Bulletin for Industry*, January, 1961.
2. H.M. (61) 5.

of the routine care of her own baby. Auxiliary nursing staff can often undertake some simple procedures, such as blanket-bathing and bedmaking, and other ward staff can do such jobs as clearing trays, changing hot-water bottles, cleaning lockers and mackintosh sheets, and moving trolleys and beds. Central supply arrangements for sterile dressings and syringes can also reduce the midwife's work.

The memorandum points out that difficulties are best overcome when there are good working relations between the medical, nursing, and midwifery staffs and suggests that these can be promoted by periodic staff meetings to discuss new techniques and procedures. Discussions between hospital and domiciliary staffs also help to make "an efficient and unified maternity service".

The Minister asks hospital boards to send him by Feb. 1, 1962, reports on their progress in dealing with this problem during 1961.

MEALS AT HOME

WITH their meals-on-wheels service, voluntary organisations have once more proved their talent for recognising a new need quickly and improvising methods of meeting it. Today over 20,000 old people receive meals in their homes from some 460 local schemes. Though these schemes are still almost all run by voluntary workers, there are signs that the service may soon become the community's responsibility. Already many of the schemes get some help from local authorities. Five local authorities have received special permission to run their own schemes, and a private member's Bill is shortly to be introduced in the House of Commons to allow all local authorities to provide mobile meals.

The National Corporation for the Care of Old People therefore thought it timely to gather together the practical experience gained by scattered local schemes during the last few years, and they have financed a survey which was carried out by the Government social survey. Miss Amelia Harris's report [1] of the survey, based on questionnaires returned by 453 schemes and interviews with 853 recipients, shows a local diversity which has made the whole movement a series of most instructive pilot experiments.

The smallest schemes cater for 3 people, the largest for 336. Some schemes operate on only one day a week, most of them on two days, a few on five or more days. Some schemes close completely during the year for periods ranging from 1 week to 19 weeks. 40% of the recipients had only one meal a week, 42% two meals, and very few had more than five meals. In some schemes the meals were cooked by members in their own homes, in others meals were obtained from the school meal service, a civic restaurant, an industrial canteen, or a local café. Almost half the recipients are over eighty, but a few are under sixty. They are usually bedfast, housebound, or disabled.

The contributions of local authorities have been as variable as other details of the schemes, and a correspondent in *The Times* lately described how a Middlesex town of 66,000 people was hampered for lack of money.[2] 16,000 meals are supplied annually at a subsidised cost of 1s. each, yet the local council's grant is only £800–£850.

The scheme has brought comfort and support to many old people, but Miss Harris's report shows that it is hampered by lack of support. First of all it is short of labour. Cooking and delivering meals can only be done by fit, fairly young women, and today these people usually have other responsibilities, especially at the time of day when the meals have to be delivered. One result of this scarcity of help is that the schemes have tended to grow up in places where voluntary help is available rather than in places where old people need meals. If the service were to become comprehensive, even at a modest estimate, meals would have to be provided for about 38,000 recipients, an increase of 85%. Again, though many old people would not want to take a meal every day in the week—some join their families at the weekend—many would like more and some would probably be grateful for a daily delivery. Similarly, though some old people can get along more easily in the summer, many would probably prefer the service not to stop for several weeks at a time when the voluntary workers, understandably, feel they must claim a break or when meals are not available from school kitchens. With the cooperation of the local authorities the service could clearly be usefully extended to many old people and to some younger people who are permanently or temporarily disabled. A possible solution, Miss Harris suggests, would be for the local authorities to provide the transport and meals and to allow the voluntary organisation to serve them and keep in touch with the recipients.

1. Meals on Wheels for Old People. 1961. Pp. 103. 7s. 6d. Outlines of a Survey on the Meals on Wheels Service. 1961. Pp. 28. 2s. 6d. Both statistical report and short general summary are obtainable from the Corporation, Nuffield Lodge, Regent's Park, London, N.W.1.
2. Broughton, E. E. *Times*, Jan. 21, 1961, p. 7.

University of Oxford

Sir Russell Brain has been awarded the Osler memorial medal.

University of Cambridge

On Dec. 20 the degree of B.CHIR. was conferred on the following:

T. C. M. Andrews, D. R. Bainbridge, J. K. Bamford, M. H. Bartlett, Barry Blackwell, R. W. Blamey, W. K. Blenkinsopp, Waalko Joost Boerema, I. F. Brockington, N. M. S. Brown, M. T. T. Bryant, Jennifer M. Charlton, Chin Cheung Chan, Hung Cheng, R. S. Dean, M. J. Denham, T. F. C. Dibble, Marjorie C. Doddridge, J. H. J. Durston, J. R. Eames, J. R. H. Fisher, A. E. Forbes, A. E. Gent, S. L. Geoghegan, D. F. Gibson, C. J. Griffiths, E. J. W. Gumpert, A. R. H. Hastie, L. J. H. E. Hayek, Michael Hayward, L. D. Heap, G. J. Johnson, A. J. Johnston, M. J. Leverton, I. C. McLellan, C. N. Mallinson, B. R. Middleton, R. S. Moore, J. P. Recordon, M. H. C. Rice, Jane M. Robson, Wendy D. Savage, R. B. Sellwood, I. S. Smith, T. H. Spreadbury, J. D. Swales, F. J. B. Taylor, J. H. Thornley, P. E. Walker, F. W. Webb, R. C. Westbury, A. J. Whitworth, E. D. G. Williams, J. D. S. Wilson, G. H. E. Woodbine, L. I. Zander.

University of London

On Dec. 14 the following degrees were awarded:

M.D.—J. G. Lewis, D. B. Moffat, Leonard Roodyn.
M.S.—N. G. Rothnie.
Ph.D. (*in the faculty of medicine*)—Norman Joels, R. P. Michael, C. M. H. Pedler.

University of Manchester

Mr. A. G. Riddell has been appointed reader in surgery, Dr. Albert Kushlick lecturer in social and preventive medicine, and Dr. C. H. Wynn lecturer in biochemistry in the department of rheumatology.

University of Nottingham

On April 27 the honorary degree of D.SC. will be conferred on Sir Howard Florey.

University of Edinburgh

The Polio Research Fund has made a grant of £25,000 to build a new research laboratory at the university's neurological unit at the Northern General Hospital, Edinburgh.

University of St. Andrews

ON Jan. 13, the degrees of M.B., CH.B. were conferred on the following:

Mary H. Drylie, Eileen J. Georgeson, J. M. Grainger, J. M. N. Hilton, M. F. Kirkman, David Rider, H. J. Royall, D. T. Williams.

Calcutta University

Dr. Subodh Mitra has been elected vice-chancellor of the university.

Royal College of Surgeons of England

Sir Russell Brock will deliver a Hunterian oration on Tuesday, Feb. 14, at 4 P.M. His subject will be Museum, Research, and the Inspiration of Hunter. Dr. H. B. G. Robinson, dean of the school of dentistry in the University of Kansas City, will give a Webb-Johnson lecture on Friday, Feb. 17, at 5 P.M. He will speak on the effects of operative procedures upon the dental pulp. Both lectures will be held at the college, Lincoln's Inn Fields, London, W.C.2.

Royal Faculty of Physicians and Surgeons of Glasgow

The following candidates have been admitted diplomates in child health:

P. M. Barnes, Doddamane Gowda Benakappa, Heymy Braude, Helen M. Dean, R. M. A. Fernando, Myrtle M. Flynn, Elinor J. Guthrie, Syed Afzal Hossein Hosseini, Helen R. McKilligin, J. R. Nairn, Margaret B. Ross, Mohammed Yusuf Siddiqui, Jagmohan Ram Srivastava, Nergesh Ratansha Surti, Lily Thomas, Sutee Ujjin, Khin Maung Win.

Lord Chancellor's Adviser

The Lord Chancellor has appointed Dr. John Harris, physician-superintendent of Claybury Hospital, Woodford Green, Essex, to be one of his medical advisers.

Conference on Atherosclerosis

This conference will be held from March 8 to 10 in the hall of the Royal Faculty of Physicians and Surgeons of Glasgow. Further details will be found in our advertisement columns.

"Nuffield Practitioners"

General-practice training appointments (registrar rates) are being offered in the Southampton, Portsmouth, or Winchester areas. Further particulars will be found in our advertisement columns.

Psychosomatic Aspects of Neoplastic Disease

An international conference on this subject, organised by the International Psychosomatic Cancer Study Group, will be held from Aug. 27 to 29 in Paris. Further particulars may be had from the U.K. representative, Dr. D. M. Kissen, Brookfield, Elm Walk, Bearsden, Glasgow.

Moorfields Research Scholarship

In 1962 this scholarship (£300) will be awarded for an essay on the clinical value of tonometry and tonography. The prize is open to all nationalities. Further particulars may be had from the director of research, Institute of Ophthalmology, Judd Street, London, W.C.1.

Family Planning Association

This Association is holding a series of lecture-discussions for senior medical students on Mondays from Feb. 6 to March 6, at 6 P.M., at B.M.A. House, Tavistock Square, London, W.C.1. The speakers will be Dr. T. F. Main (Normal Psychosexual Development and Marital Adjustment); Dr. Eleanor Mears (Psychosexual Difficulties in the Wife); Dr. Clifford Allen (Sex Difficulties and Perversions in the Husband); Dr. Stephen Pasmore (Sexual Difficulties Presenting in General Practice); and Dr. Sylvia Dawkins (Giving Contraceptive Advice). Admission will be free.

International Conference on Military Medicine

The Office International de Documentation de Médecine Militaire is to hold a conference in Athens from Sept. 19 to 22. The programme will include discussions on pulmonary tuberculosis in Armed Forces; nurse-teaching methods for the care of war-time casualties; and blood-groups and identity discs. Further particulars may be had from the secretariat of the conference, État-Major Général de l'Armée hellénique, Direction du Service de Santé de l'Armée, Athens, Greece.

Lady Tata Memorial Trust

The trustees of this Trust invite applications for grants, scholarships, and fellowships for research on diseases of the blood, with special reference to leukæmia.

Programmes of research on any aspect of malignant disease which may throw light on problems of leukæmia will be considered, and the trustees specially wish to encourage studies of the leukæmogenic viruses in mammals, the epidemiology and natural history of leukæmia, and the genetical and cytological aspects. The awards are open to investigators of any nationality, working either in their own institutions or in other centres abroad, in any country where payment can be made. Forms of application may be had from the secretary of the (European) scientific advisory committee of the Trust, Chester Beatty Research Institute, Fulham Road, London, S.W.3, and must be submitted before March 31.

Surgeon Captain W. J. M. Sadler, R.N., has been appointed honorary surgeon to the Queen in succession to Surgeon Rear-Admiral D. F. Walsh.

At a meeting of the Medical Electronics Discussion Group on Friday, Feb. 3, at 6 P.M., at the Institute of Electrical Engineers, Savoy Place, London, W.C.2, there will be a discussion on recent technical developments in eye-movement recording. The opening speakers will be Dr. P. A. Merton and Dr. Cyril Rashbass.

A meeting of the North of England Otolaryngological Society will be held on Saturday, Feb. 18, at 2 P.M., in Sheffield.

On Call to a Nation, a 75-minute study of the National Health Service as seen through the eyes of doctors, which was televised by the B.B.C. in October, 1958, has been acquired by the Central Film Library, and is available for hire on a 16-mm. sound-projector. Further particulars may be had from the Library, Government Building, Bromyard Avenue, Acton, London, W.3.

CORRIGENDUM: *Influence of Diet on Serum-triglycerides.*—In the article by Dr. A. Antonis and Dr. I. Bersohn (Jan. 7, p. 3) the new sentence on line 15 of the second paragraph under "experimental procedure" (p. 4) should have opened with the words: "A 120 cm. [*not* mm.] glass column . . ."

Diary of the Week

JAN. 29 TO FEB. 4

Monday, 30th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. J. F. Goodwin: Bacterial Endocarditis.

Tuesday, 31st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. H. E. M. Kay: Transplantation of Hæmopoietic Cells.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. G. C. Wells: Tumours arising in the Dermis, excluding Moles and Melanomata.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. (Wright-Fleming Institute.) Dr. A. White Franklin: Care of the Premature Baby.

ROYAL STATISTICAL SOCIETY
6.15 P.M. (London School of Hygiene and Tropical Medicine.) *Medical Section.* Mr. D. J. Newell: Demand for Hospital Beds.

Wednesday, 1st

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. F. G. J. Hayhoe: Cytology of Leukæmic Cells.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Eosinophilic Granulomas of the Skin.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. F. P. Lee Lander: Diagnosis of Carcinoma of the Lung.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Dr. Imrich Friedmann, Dr. D. A. Osborn, Dr. A. L. Jeanes: Clinical Pathological Conference.

ASSURANCE MEDICAL SOCIETY
5 P.M. (11, Chandos Street, London, W.1.) Dr. H. N. Collier: If Not Accuracy, At Least Consistency. (Presidential address.)

MIDLAND MEDICAL SOCIETY
8.30 P.M. (Birmingham Medical Institute, 36, Harborne Road, Birmingham, 15.) Dr. E. G. L. Bywaters: Neuropathic Joint Disease and Rheumatoid Neuropathies.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) *Medicine.* Dr. John Badenoch: Diagnosis and Management of the Malabsorption Syndrome.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow, C.2
5 P.M. Prof. J. F. Nuboer (Utrecht): Surgical Treatment of Tumours of Duodeno-Pancreas. (Lock lecture.)

Thursday, 2nd

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5.30 P.M. Prof. Victor Lambert: Malignant Melanoma of the Nose.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. C. E. Ford: Interrelationship of Nucleus and Cytoplasm.

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Mr. F. W. Holdsworth: Injuries to the Spine.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Dr. W. M. Court Brown: Cytogenetic Studies in Human Leukæmias.

Friday, 3rd

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Dr. D. C. Sabiston, Jr. (Baltimore): Surgical Aspects of Coronary Artery Disease.
4 P.M. Prof. John McMichael: Hypertension.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
2.30 P.M. *Laryngology.* Mr. C. P. Wilson, Mr. R. S. Lewis, Dr. Frank Ellis, Dr. I. Simson Hall: Treatment of Intrinsic Carcinoma of the Larynx.
5.30 P.M. *Anæsthetics.* Mr. L. P. Le Quesne, Dr. P. J. Horsey: Fluid and Electrolyte Problems in Abdominal Emergencies.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. Kenneth McLay: Surgical Treatment of Deafness.

Saturday, 4th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
NOON. Prof. D. R. Griffin (Harvard University): Echolocation in Bats, with Special Reference to Insect Catching.

MIDLAND THORACIC SOCIETY
3 P.M. (Birmingham Medical Institute.) Mr. L. D. Abrams, Dr. W. A. Hudson: Heart Block and Its Management.